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<b>(21) International Application Number:</b> PCT/US99/15838 <b>(22) International Filing Date:</b> 14 July 1999 (14.07.99)		<b>(74) Agents:</b> MAKI, David, J. et al.; Seed and Berry LLP, 6300 Columbia, 701 Fifth Avenue, Seattle, WA 98104-7092 (US).	
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<b>(54) Title:</b> COMPOSITIONS AND METHODS FOR THERAPY AND DIAGNOSIS OF PROSTATE CANCER			
<b>(57) Abstract</b> <p>Compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer, are disclosed. Compositions may comprise one or more prostate tumor proteins, immunogenic portions thereof, or polynucleotides that encode such portions. Alternatively, a therapeutic composition may comprise an antigen presenting cell that expresses a prostate tumor protein, or a T cell that is specific for cells expressing such a protein. Such compositions may be used, for example, for the prevention and treatment of diseases such as prostate cancer. Diagnostic methods based on detecting a prostate tumor protein, or mRNA encoding such a protein, in a sample are also provided.</p>			

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## COMPOSITIONS AND METHODS FOR THERAPY AND DIAGNOSIS OF PROSTATE CANCER

### TECHNICAL FIELD

The present invention relates generally to therapy and diagnosis of cancer, such as prostate cancer. The invention is more specifically related to polypeptides comprising at least a portion of a prostate tumor protein, and to polynucleotides encoding such polypeptides. Such polypeptides and polynucleotides may be used in vaccines and pharmaceutical compositions for prevention and treatment of prostate cancer, and for the diagnosis and monitoring of such cancers.

### BACKGROUND OF THE INVENTION

Prostate cancer is the most common form of cancer among males, with an estimated incidence of 30% in men over the age of 50. Overwhelming clinical evidence shows that human prostate cancer has the propensity to metastasize to bone, and the disease appears to progress inevitably from androgen dependent to androgen refractory status, leading to increased patient mortality. This prevalent disease is currently the second leading cause of cancer death among men in the U.S.

In spite of considerable research into therapies for the disease, prostate cancer remains difficult to treat. Commonly, treatment is based on surgery and/or radiation therapy, but these methods are ineffective in a significant percentage of cases. Two previously identified prostate specific proteins - prostate specific antigen (PSA) and prostatic acid phosphatase (PAP) - have limited therapeutic and diagnostic potential. For example, PSA levels do not always correlate well with the presence of prostate cancer, being positive in a percentage of non-prostate cancer cases, including benign prostatic hyperplasia (BPH). Furthermore, PSA measurements correlate with prostate volume, and do not indicate the level of metastasis.

In spite of considerable research into therapies for these and other cancers, prostate cancer remains difficult to diagnose and treat effectively. Accordingly, there is a need in the art for improved methods for detecting and treating such cancers. The present invention fulfills these needs and further provides other related advantages.

### SUMMARY OF THE INVENTION

Briefly stated, the present invention provides compositions and methods for the diagnosis and therapy of cancer, such as prostate cancer. In one aspect, the present

invention provides polypeptides comprising at least a portion of a prostate tumor protein, or a variant thereof. Certain portions and other variants are immunogenic, such that the ability of the variant to react with antigen-specific antisera is not substantially diminished. Within certain embodiments, the polypeptide comprises at least an immunogenic portion of a prostate tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of: (a) sequences recited in any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472; (b) sequences that hybridize to any of the foregoing sequences under moderately stringent conditions; and (c) complements of any of the sequence of (a) or (b). In certain specific embodiments, such a polypeptide comprises at least a portion, or variant thereof, of a tumor protein that includes an amino acid sequence selected from the group consisting of sequences recited in any one of SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380 and 383.

The present invention further provides polynucleotides that encode a polypeptide as described above, or a portion thereof (such as a portion encoding at least 15 amino acid residues of a prostate tumor protein), expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

Within other aspects, the present invention provides pharmaceutical compositions comprising a polypeptide or polynucleotide as described above and a physiologically acceptable carrier.

Within a related aspect of the present invention, vaccines are provided. Such vaccines comprise a polypeptide or polynucleotide as described above and a non-specific immune response enhancer.

The present invention further provides pharmaceutical compositions that comprise: (a) an antibody or antigen-binding fragment thereof that specifically binds to a prostate tumor protein; and (b) a physiologically acceptable carrier.

Within further aspects, the present invention provides pharmaceutical compositions comprising: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a pharmaceutically acceptable carrier or excipient. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B cells.

Within related aspects, vaccines are provided that comprise: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a non-specific immune response enhancer.

The present invention further provides, in other aspects, fusion proteins that comprise at least one polypeptide as described above, as well as polynucleotides encoding such fusion proteins.



Within related aspects, pharmaceutical compositions comprising a fusion protein, or a polynucleotide encoding a fusion protein, in combination with a physiologically acceptable carrier are provided.

Vaccines are further provided, within other aspects, that comprise a fusion protein, or a polynucleotide encoding a fusion protein, in combination with a non-specific immune response enhancer.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient a pharmaceutical composition or vaccine as recited above.

The present invention further provides, within other aspects, methods for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a prostate tumor protein, wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the protein from the sample.

Within related aspects, methods are provided for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated as described above.

Methods are further provided, within other aspects, for stimulating and/or expanding T cells specific for a prostate tumor protein, comprising contacting T cells with one or more of: (i) a polypeptide as described above; (ii) a polynucleotide encoding such a polypeptide; and/or (iii) an antigen presenting cell that expresses such a polypeptide; under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells. Isolated T cell populations comprising T cells prepared as described above are also provided.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population as described above.

The present invention further provides methods for inhibiting the development of a cancer in a patient, comprising the steps of: (a) incubating CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient with one or more of: (i) a polypeptide comprising at least an immunogenic portion of a prostate tumor protein; (ii) a polynucleotide encoding such a polypeptide; and (iii) an antigen-presenting cell that expressed such a polypeptide; and (b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient. Proliferated cells may, but need not, be cloned prior to administration to the patient.

Within further aspects, the present invention provides methods for determining the presence or absence of a cancer in a patient, comprising: (a) contacting a biological sample obtained from a patient with a binding agent that binds to a polypeptide as recited

above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and (c) comparing the amount of polypeptide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within preferred embodiments, the binding agent is an antibody, more preferably a monoclonal antibody. The cancer may be prostate cancer.

The present invention also provides, within other aspects, methods for monitoring the progression of a cancer in a patient. Such methods comprise the steps of: (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polypeptide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

The present invention further provides, within other aspects, methods for determining the presence or absence of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate tumor protein; (b) detecting in the sample a level of a polynucleotide, preferably mRNA, that hybridizes to the oligonucleotide; and (c) comparing the level of polynucleotide that hybridizes to the oligonucleotide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within certain embodiments, the amount of mRNA is detected via polymerase chain reaction using, for example, at least one oligonucleotide primer that hybridizes to a polynucleotide encoding a polypeptide as recited above, or a complement of such a polynucleotide. Within other embodiments, the amount of mRNA is detected using a hybridization technique, employing an oligonucleotide probe that hybridizes to a polynucleotide that encodes a polypeptide as recited above, or a complement of such a polynucleotide.

In related aspects, methods are provided for monitoring the progression of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate tumor protein; (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polynucleotide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

Within further aspects, the present invention provides antibodies, such as monoclonal antibodies, that bind to a polypeptide as described above, as well as diagnostic

kits comprising such antibodies. Diagnostic kits comprising one or more oligonucleotide probes or primers as described above are also provided.

These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached drawings. All references disclosed herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

#### BRIEF DESCRIPTION OF THE DRAWINGS AND SEQUENCE IDENTIFIERS

Figure 1 illustrates the ability of T cells to kill fibroblasts expressing the representative prostate tumor polypeptide P502S, as compared to control fibroblasts. The percentage lysis is shown as a series of effector:target ratios, as indicated.

Figures 2A and 2B illustrate the ability of T cells to recognize cells expressing the representative prostate tumor polypeptide P502S. In each case, the number of  $\gamma$ -interferon spots is shown for different numbers of responders. In Figure 2A, data is presented for fibroblasts pulsed with the P2S-12 peptide, as compared to fibroblasts pulsed with a control E75 peptide. In Figure 2B, data is presented for fibroblasts expressing P502S, as compared to fibroblasts expressing HER-2/*neu*.

Figure 3 represents a peptide competition binding assay showing that the P1S#10 peptide, derived from P501S, binds HLA-A2. Peptide P1S#10 inhibits HLA-A2 restricted presentation of fluM58 peptide to CTL clone D150M58 in TNF release bioassay. D150M58 CTL is specific for the HLA-A2 binding influenza matrix peptide fluM58.

Figure 4 illustrates the ability of T cell lines generated from P1S#10 immunized mice to specifically lyse P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat A2Kb targets, as compared to EGFP-transduced Jurkat A2Kb. The percent lysis is shown as a series of effector to target ratios, as indicated.

Figure 5 illustrates the ability of a T cell clone to recognize and specifically lyse Jurkat A2Kb cells expressing the representative prostate tumor polypeptide P501S, thereby demonstrating that the P1S#10 peptide may be a naturally processed epitope of the P501S polypeptide.

Figures 6A and 6B are graphs illustrating the specificity of a CD8<sup>+</sup> cell line (3A-1) for a representative prostate tumor antigen (P501S). Figure 6A shows the results of a <sup>51</sup>Cr release assay. The percent specific lysis is shown as a series of effector:target ratios, as indicated. Figure 6B shows the production of interferon-gamma by 3A-1 cells stimulated with autologous B-LCL transduced with P501S, at varying effector:target ratios as indicated.

SEQ ID NO: 1 is the determined cDNA sequence for F1-13

SEQ ID NO: 2 is the determined 3' cDNA sequence for F1-12

SEQ ID NO: 3 is the determined 5' cDNA sequence for F1-12  
SEQ ID NO: 4 is the determined 3' cDNA sequence for F1-16  
SEQ ID NO: 5 is the determined 3' cDNA sequence for H1-1  
SEQ ID NO: 6 is the determined 3' cDNA sequence for H1-9  
SEQ ID NO: 7 is the determined 3' cDNA sequence for H1-4  
SEQ ID NO: 8 is the determined 3' cDNA sequence for J1-17  
SEQ ID NO: 9 is the determined 5' cDNA sequence for J1-17  
SEQ ID NO: 10 is the determined 3' cDNA sequence for L1-12  
SEQ ID NO: 11 is the determined 5' cDNA sequence for L1-12  
SEQ ID NO: 12 is the determined 3' cDNA sequence for N1-1862  
SEQ ID NO: 13 is the determined 5' cDNA sequence for N1-1862  
SEQ ID NO: 14 is the determined 3' cDNA sequence for J1-13  
SEQ ID NO: 15 is the determined 5' cDNA sequence for J1-13  
SEQ ID NO: 16 is the determined 3' cDNA sequence for J1-19  
SEQ ID NO: 17 is the determined 5' cDNA sequence for J1-19  
SEQ ID NO: 18 is the determined 3' cDNA sequence for J1-25  
SEQ ID NO: 19 is the determined 5' cDNA sequence for J1-25  
SEQ ID NO: 20 is the determined 5' cDNA sequence for J1-24  
SEQ ID NO: 21 is the determined 3' cDNA sequence for J1-24  
SEQ ID NO: 22 is the determined 5' cDNA sequence for K1-58  
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SEQ ID NO: 24 is the determined 5' cDNA sequence for K1-63  
SEQ ID NO: 25 is the determined 3' cDNA sequence for K1-63  
SEQ ID NO: 26 is the determined 5' cDNA sequence for L1-4  
SEQ ID NO: 27 is the determined 3' cDNA sequence for L1-4  
SEQ ID NO: 28 is the determined 5' cDNA sequence for L1-14  
SEQ ID NO: 29 is the determined 3' cDNA sequence for L1-14  
SEQ ID NO: 30 is the determined 3' cDNA sequence for J1-12  
SEQ ID NO: 31 is the determined 3' cDNA sequence for J1-16  
SEQ ID NO: 32 is the determined 3' cDNA sequence for J1-21  
SEQ ID NO: 33 is the determined 3' cDNA sequence for K1-48  
SEQ ID NO: 34 is the determined 3' cDNA sequence for K1-55  
SEQ ID NO: 35 is the determined 3' cDNA sequence for L1-2  
SEQ ID NO: 36 is the determined 3' cDNA sequence for L1-6  
SEQ ID NO: 37 is the determined 3' cDNA sequence for N1-1858  
SEQ ID NO: 38 is the determined 3' cDNA sequence for N1-1860  
SEQ ID NO: 39 is the determined 3' cDNA sequence for N1-1861

SEQ ID NO: 40 is the determined 3' cDNA sequence for N1-1864  
SEQ ID NO: 41 is the determined cDNA sequence for P5  
SEQ ID NO: 42 is the determined cDNA sequence for P8  
SEQ ID NO: 43 is the determined cDNA sequence for P9  
SEQ ID NO: 44 is the determined cDNA sequence for P18  
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SEQ ID NO: 46 is the determined cDNA sequence for P29  
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SEQ ID NO: 55 is the determined cDNA sequence for P50  
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SEQ ID NO: 57 is the determined cDNA sequence for P55  
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SEQ ID NO: 71 is the determined cDNA sequence for V1-3692  
SEQ ID NO: 72 is the determined cDNA sequence for 1A-3905  
SEQ ID NO: 73 is the determined cDNA sequence for V1-3686  
SEQ ID NO: 74 is the determined cDNA sequence for R1-2330  
SEQ ID NO: 75 is the determined cDNA sequence for 1B-3976  
SEQ ID NO: 76 is the determined cDNA sequence for V1-3679

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SEQ ID NO: 81 is the determined cDNA sequence for 1G-4734  
SEQ ID NO: 82 is the determined cDNA sequence for 1H-4774  
SEQ ID NO: 83 is the determined cDNA sequence for 1H-4781  
SEQ ID NO: 84 is the determined cDNA sequence for 1H-4785  
SEQ ID NO: 85 is the determined cDNA sequence for 1H-4787  
SEQ ID NO: 86 is the determined cDNA sequence for 1H-4796  
SEQ ID NO: 87 is the determined cDNA sequence for 1I-4807  
SEQ ID NO: 88 is the determined cDNA sequence for 1I-4810  
SEQ ID NO: 89 is the determined cDNA sequence for 1I-4811  
SEQ ID NO: 90 is the determined cDNA sequence for 1J-4876  
SEQ ID NO: 91 is the determined cDNA sequence for 1K-4884  
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SEQ ID NO: 93 is the determined cDNA sequence for 1G-4761  
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SEQ ID NO: 107 is the determined full length cDNA sequence for F1-12 (also referred to as P504S)  
SEQ ID NO: 108 is the predicted amino acid sequence for F1-12  
SEQ ID NO: 109 is the determined full length cDNA sequence for J1-17  
SEQ ID NO: 110 is the determined full length cDNA sequence for L1-12  
SEQ ID NO: 111 is the determined full length cDNA sequence for N1-1862  
SEQ ID NO: 112 is the predicted amino acid sequence for J1-17

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SEQ ID NO: 172 is the predicted amino acid sequence for P703P-DE1  
SEQ ID NO: 173 is the determined cDNA sequence for P703P-DE2  
SEQ ID NO: 174 is the determined cDNA sequence for P703P-DE6  
SEQ ID NO: 175 is the determined cDNA sequence for P703P-DE13  
SEQ ID NO: 176 is the predicted amino acid sequence for P703P-DE13  
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SEQ ID NO: 202 is the determined extended cDNA sequence for 1D-4288  
SEQ ID NO: 203 is the determined extended cDNA sequence for 1D-4283  
SEQ ID NO: 204 is the determined extended cDNA sequence for 1D-4304  
SEQ ID NO: 205 is the determined extended cDNA sequence for 1D-4296  
SEQ ID NO: 206 is the determined extended cDNA sequence for 1D-4280  
SEQ ID NO: 207 is the determined cDNA sequence for 10-d8fwd  
SEQ ID NO: 208 is the determined cDNA sequence for 10-H10con  
SEQ ID NO: 209 is the determined cDNA sequence for 11-C8rev  
SEQ ID NO: 210 is the determined cDNA sequence for 7.g6fwd  
SEQ ID NO: 211 is the determined cDNA sequence for 7.g6rev  
SEQ ID NO: 212 is the determined cDNA sequence for 8-b5fwd  
SEQ ID NO: 213 is the determined cDNA sequence for 8-b5rev  
SEQ ID NO: 214 is the determined cDNA sequence for 8-b6fwd  
SEQ ID NO: 215 is the determined cDNA sequence for 8-b6 rev  
SEQ ID NO: 216 is the determined cDNA sequence for 8-d4fwd  
SEQ ID NO: 217 is the determined cDNA sequence for 8-d9rev  
SEQ ID NO: 218 is the determined cDNA sequence for 8-g3fwd  
SEQ ID NO: 219 is the determined cDNA sequence for 8-g3rev  
SEQ ID NO: 220 is the determined cDNA sequence for 8-h11rev  
SEQ ID NO: 221 is the determined cDNA sequence for g-f12fwd  
SEQ ID NO: 222 is the determined cDNA sequence for g-f3rev  
SEQ ID NO: 223 is the determined cDNA sequence for P509S

SEQ ID NO: 224 is the determined cDNA sequence for P510S  
SEQ ID NO: 225 is the determined cDNA sequence for P703DE5  
SEQ ID NO: 226 is the determined cDNA sequence for 9-A11  
SEQ ID NO: 227 is the determined cDNA sequence for 8-C6  
SEQ ID NO: 228 is the determined cDNA sequence for 8-H7  
SEQ ID NO: 229 is the determined cDNA sequence for JPTPN13  
SEQ ID NO: 230 is the determined cDNA sequence for JPTPN14  
SEQ ID NO: 231 is the determined cDNA sequence for JPTPN23  
SEQ ID NO: 232 is the determined cDNA sequence for JPTPN24  
SEQ ID NO: 233 is the determined cDNA sequence for JPTPN25  
SEQ ID NO: 234 is the determined cDNA sequence for JPTPN30  
SEQ ID NO: 235 is the determined cDNA sequence for JPTPN34  
SEQ ID NO: 236 is the determined cDNA sequence for PTPN35  
SEQ ID NO: 237 is the determined cDNA sequence for JPTPN36  
SEQ ID NO: 238 is the determined cDNA sequence for JPTPN38  
SEQ ID NO: 239 is the determined cDNA sequence for JPTPN39  
SEQ ID NO: 240 is the determined cDNA sequence for JPTPN40  
SEQ ID NO: 241 is the determined cDNA sequence for JPTPN41  
SEQ ID NO: 242 is the determined cDNA sequence for JPTPN42  
SEQ ID NO: 243 is the determined cDNA sequence for JPTPN45  
SEQ ID NO: 244 is the determined cDNA sequence for JPTPN46  
SEQ ID NO: 245 is the determined cDNA sequence for JPTPN51  
SEQ ID NO: 246 is the determined cDNA sequence for JPTPN56  
SEQ ID NO: 247 is the determined cDNA sequence for PTPN64  
SEQ ID NO: 248 is the determined cDNA sequence for JPTPN65  
SEQ ID NO: 249 is the determined cDNA sequence for JPTPN67  
SEQ ID NO: 250 is the determined cDNA sequence for JPTPN76  
SEQ ID NO: 251 is the determined cDNA sequence for JPTPN84  
SEQ ID NO: 252 is the determined cDNA sequence for JPTPN85  
SEQ ID NO: 253 is the determined cDNA sequence for JPTPN86  
SEQ ID NO: 254 is the determined cDNA sequence for JPTPN87  
SEQ ID NO: 255 is the determined cDNA sequence for JPTPN88  
SEQ ID NO: 256 is the determined cDNA sequence for JP1F1  
SEQ ID NO: 257 is the determined cDNA sequence for JP1F2  
SEQ ID NO: 258 is the determined cDNA sequence for JP1C2  
SEQ ID NO: 259 is the determined cDNA sequence for JP1B1  
SEQ ID NO: 260 is the determined cDNA sequence for JP1B2

SEQ ID NO: 261 is the determined cDNA sequence for JP1D3  
SEQ ID NO: 262 is the determined cDNA sequence for JP1A4  
SEQ ID NO: 263 is the determined cDNA sequence for JP1F5  
SEQ ID NO: 264 is the determined cDNA sequence for JP1E6  
SEQ ID NO: 265 is the determined cDNA sequence for JP1D6  
SEQ ID NO: 266 is the determined cDNA sequence for JP1B5  
SEQ ID NO: 267 is the determined cDNA sequence for JP1A6  
SEQ ID NO: 268 is the determined cDNA sequence for JP1E8  
SEQ ID NO: 269 is the determined cDNA sequence for JP1D7  
SEQ ID NO: 270 is the determined cDNA sequence for JP1D9  
SEQ ID NO: 271 is the determined cDNA sequence for JP1C10  
SEQ ID NO: 272 is the determined cDNA sequence for JP1A9  
SEQ ID NO: 273 is the determined cDNA sequence for JP1F12  
SEQ ID NO: 274 is the determined cDNA sequence for JP1E12  
SEQ ID NO: 275 is the determined cDNA sequence for JP1D11  
SEQ ID NO: 276 is the determined cDNA sequence for JP1C11  
SEQ ID NO: 277 is the determined cDNA sequence for JP1C12  
SEQ ID NO: 278 is the determined cDNA sequence for JP1B12  
SEQ ID NO: 279 is the determined cDNA sequence for JP1A12  
SEQ ID NO: 280 is the determined cDNA sequence for JP8G2  
SEQ ID NO: 281 is the determined cDNA sequence for JP8H1  
SEQ ID NO: 282 is the determined cDNA sequence for JP8H2  
SEQ ID NO: 283 is the determined cDNA sequence for JP8A3  
SEQ ID NO: 284 is the determined cDNA sequence for JP8A4  
SEQ ID NO: 285 is the determined cDNA sequence for JP8C3  
SEQ ID NO: 286 is the determined cDNA sequence for JP8G4  
SEQ ID NO: 287 is the determined cDNA sequence for JP8B6  
SEQ ID NO: 288 is the determined cDNA sequence for JP8D6  
SEQ ID NO: 289 is the determined cDNA sequence for JP8F5  
SEQ ID NO: 290 is the determined cDNA sequence for JP8A8  
SEQ ID NO: 291 is the determined cDNA sequence for JP8C7  
SEQ ID NO: 292 is the determined cDNA sequence for JP8D7  
SEQ ID NO: 293 is the determined cDNA sequence for P8D8  
SEQ ID NO: 294 is the determined cDNA sequence for JP8E7  
SEQ ID NO: 295 is the determined cDNA sequence for JP8F8  
SEQ ID NO: 296 is the determined cDNA sequence for JP8G8  
SEQ ID NO: 297 is the determined cDNA sequence for JP8B10

SEQ ID NO: 298 is the determined cDNA sequence for JP8C10  
SEQ ID NO: 299 is the determined cDNA sequence for JP8E9  
SEQ ID NO: 300 is the determined cDNA sequence for JP8E10  
SEQ ID NO: 301 is the determined cDNA sequence for JP8F9  
SEQ ID NO: 302 is the determined cDNA sequence for JP8H9  
SEQ ID NO: 303 is the determined cDNA sequence for JP8C12  
SEQ ID NO: 304 is the determined cDNA sequence for JP8E11  
SEQ ID NO: 305 is the determined cDNA sequence for JP8E12  
SEQ ID NO: 306 is the amino acid sequence for the peptide PS2#12  
SEQ ID NO: 307 is the determined cDNA sequence for P711P  
SEQ ID NO: 308 is the determined cDNA sequence for P712P  
SEQ ID NO: 309 is the determined cDNA sequence for CLONE23  
SEQ ID NO: 310 is the determined cDNA sequence for P774P  
SEQ ID NO: 311 is the determined cDNA sequence for P775P  
SEQ ID NO: 312 is the determined cDNA sequence for P715P  
SEQ ID NO: 313 is the determined cDNA sequence for P710P  
SEQ ID NO: 314 is the determined cDNA sequence for P767P  
SEQ ID NO: 315 is the determined cDNA sequence for P768P  
SEQ ID NO: 316-325 are the determined cDNA sequences of previously isolated genes  
SEQ ID NO: 326 is the determined cDNA sequence for P703PDE5  
SEQ ID NO: 327 is the predicted amino acid sequence for P703PDE5  
SEQ ID NO: 328 is the determined cDNA sequence for P703P6.26  
SEQ ID NO: 329 is the predicted amino acid sequence for P703P6.26  
SEQ ID NO: 330 is the determined cDNA sequence for P703PX-23  
SEQ ID NO: 331 is the predicted amino acid sequence for P703PX-23  
SEQ ID NO: 332 is the determined full length cDNA sequence for P509S  
SEQ ID NO: 333 is the determined extended cDNA sequence for P707P (also referred to as 11-C9)  
SEQ ID NO: 334 is the determined cDNA sequence for P714P  
SEQ ID NO: 335 is the determined cDNA sequence for P705P (also referred to as 9-F3)  
SEQ ID NO: 336 is the predicted amino acid sequence for P705P  
SEQ ID NO: 337 is the amino acid sequence of the peptide P1S#10  
SEQ ID NO: 338 is the amino acid sequence of the peptide p5  
SEQ ID NO: 339 is the predicted amino acid sequence of P509S  
SEQ ID NO: 340 is the determined cDNA sequence for P778P  
SEQ ID NO: 341 is the determined cDNA sequence for P786P  
SEQ ID NO: 342 is the determined cDNA sequence for P789P

SEQ ID NO: 343 is the determined cDNA sequence for a clone showing homology to Homo sapiens MM46 mRNA

SEQ ID NO: 344 is the determined cDNA sequence for a clone showing homology to Homo sapiens TNF-alpha stimulated ABC protein (ABC50) mRNA

SEQ ID NO: 345 is the determined cDNA sequence for a clone showing homology to Homo sapiens mRNA for E-cadherin

SEQ ID NO: 346 is the determined cDNA sequence for a clone showing homology to Human nuclear-encoded mitochondrial serine hydroxymethyltransferase (SHMT)

SEQ ID NO: 347 is the determined cDNA sequence for a clone showing homology to Homo sapiens natural resistance-associated macrophage protein2 (NRAMP2)

SEQ ID NO: 348 is the determined cDNA sequence for a clone showing homology to Homo sapiens phosphoglucosyltransferase-related protein (PGMRP)

SEQ ID NO: 349 is the determined cDNA sequence for a clone showing homology to Human mRNA for proteosome subunit p40

SEQ ID NO: 350 is the determined cDNA sequence for P777P

SEQ ID NO: 351 is the determined cDNA sequence for P779P

SEQ ID NO: 352 is the determined cDNA sequence for P790P

SEQ ID NO: 353 is the determined cDNA sequence for P784P

SEQ ID NO: 354 is the determined cDNA sequence for P776P

SEQ ID NO: 355 is the determined cDNA sequence for P780P

SEQ ID NO: 356 is the determined cDNA sequence for P544S

SEQ ID NO: 357 is the determined cDNA sequence for P745S

SEQ ID NO: 358 is the determined cDNA sequence for P782P

SEQ ID NO: 359 is the determined cDNA sequence for P783P

SEQ ID NO: 360 is the determined cDNA sequence for unknown 17984

SEQ ID NO: 361 is the determined cDNA sequence for P787P

SEQ ID NO: 362 is the determined cDNA sequence for P788P

SEQ ID NO: 363 is the determined cDNA sequence for unknown 17994

SEQ ID NO: 364 is the determined cDNA sequence for P781P

SEQ ID NO: 365 is the determined cDNA sequence for P785P

SEQ ID NO: 366-375 are the determined cDNA sequences for splice variants of B305D.

SEQ ID NO: 376 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 366.

SEQ ID NO: 377 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 372.

SEQ ID NO: 378 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 373.

SEQ ID NO: 379 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 374.

SEQ ID NO: 380 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 375.

SEQ ID NO: 381 is the determined cDNA sequence for B716P.

SEQ ID NO: 382 is the determined full-length cDNA sequence for P711P.

SEQ ID NO: 383 is the predicted amino acid sequence for P711P.

SEQ ID NO: 384 is the cDNA sequence for P1000C.

SEQ ID NO: 385 is the cDNA sequence for CGI-82.

SEQ ID NO: 386 is the cDNA sequence for 23320.

SEQ ID NO: 387 is the cDNA sequence for CGI-69.

SEQ ID NO: 388 is the cDNA sequence for L-iditol-2-dehydrogenase.

SEQ ID NO: 389 is the cDNA sequence for 23379.

SEQ ID NO: 390 is the cDNA sequence for 23381.

SEQ ID NO: 391 is the cDNA sequence for KIAA0122.

SEQ ID NO: 392 is the cDNA sequence for 23399.

SEQ ID NO: 393 is the cDNA sequence for a previously identified gene.

SEQ ID NO: 394 is the cDNA sequence for HCLBP.

SEQ ID NO: 395 is the cDNA sequence for transglutaminase.

SEQ ID NO: 396 is the cDNA sequence for a previously identified gene.

SEQ ID NO: 397 is the cDNA sequence for PAP.

SEQ ID NO: 398 is the cDNA sequence for Ets transcription factor PDEF.

SEQ ID NO: 399 is the cDNA sequence for hTGR.

SEQ ID NO: 400 is the cDNA sequence for KIAA0295.

SEQ ID NO: 401 is the cDNA sequence for 22545.

SEQ ID NO: 402 is the cDNA sequence for 22547.

SEQ ID NO: 403 is the cDNA sequence for 22548.

SEQ ID NO: 404 is the cDNA sequence for 22550.

SEQ ID NO: 405 is the cDNA sequence for 22551.

SEQ ID NO: 406 is the cDNA sequence for 22552.

SEQ ID NO: 407 is the cDNA sequence for 22553.

SEQ ID NO: 408 is the cDNA sequence for 22558.

SEQ ID NO: 409 is the cDNA sequence for 22562.

SEQ ID NO: 410 is the cDNA sequence for 22565.

SEQ ID NO: 411 is the cDNA sequence for 22567.

SEQ ID NO: 412 is the cDNA sequence for 22568.

SEQ ID NO: 413 is the cDNA sequence for 22570.

SEQ ID NO:414 is the cDNA sequence for 22571.  
SEQ ID NO:415 is the cDNA sequence for 22572.  
SEQ ID NO:416 is the cDNA sequence for 22573.  
SEQ ID NO:417 is the cDNA sequence for 22573.  
SEQ ID NO:418 is the cDNA sequence for 22575.  
SEQ ID NO:419 is the cDNA sequence for 22580.  
SEQ ID NO:420 is the cDNA sequence for 22581.  
SEQ ID NO:421 is the cDNA sequence for 22582.  
SEQ ID NO:422 is the cDNA sequence for 22583.  
SEQ ID NO:423 is the cDNA sequence for 22584.  
SEQ ID NO:424 is the cDNA sequence for 22585.  
SEQ ID NO:425 is the cDNA sequence for 22586.  
SEQ ID NO:426 is the cDNA sequence for 22587.  
SEQ ID NO:427 is the cDNA sequence for 22588.  
SEQ ID NO:428 is the cDNA sequence for 22589.  
SEQ ID NO:429 is the cDNA sequence for 22590.  
SEQ ID NO:430 is the cDNA sequence for 22591.  
SEQ ID NO:431 is the cDNA sequence for 22592.  
SEQ ID NO:432 is the cDNA sequence for 22593.  
SEQ ID NO:433 is the cDNA sequence for 22594.  
SEQ ID NO:434 is the cDNA sequence for 22595.  
SEQ ID NO:435 is the cDNA sequence for 22596.  
SEQ ID NO:436 is the cDNA sequence for 22847.  
SEQ ID NO:437 is the cDNA sequence for 22848.  
SEQ ID NO:438 is the cDNA sequence for 22849.  
SEQ ID NO:439 is the cDNA sequence for 22851.  
SEQ ID NO:440 is the cDNA sequence for 22852.  
SEQ ID NO:441 is the cDNA sequence for 22853.  
SEQ ID NO:442 is the cDNA sequence for 22854.  
SEQ ID NO:443 is the cDNA sequence for 22855.  
SEQ ID NO:444 is the cDNA sequence for 22856.  
SEQ ID NO:445 is the cDNA sequence for 22857.  
SEQ ID NO:446 is the cDNA sequence for 23601.  
SEQ ID NO:447 is the cDNA sequence for 23602.  
SEQ ID NO:448 is the cDNA sequence for 23605.  
SEQ ID NO:449 is the cDNA sequence for 23606.  
SEQ ID NO:450 is the cDNA sequence for 23612.

SEQ ID NO:451 is the cDNA sequence for 23614.  
SEQ ID NO:452 is the cDNA sequence for 23618.  
SEQ ID NO:453 is the cDNA sequence for 23622.  
SEQ ID NO:454 is the cDNA sequence for folate hydrolase.  
SEQ ID NO:455 is the cDNA sequence for LIM protein.  
SEQ ID NO:456 is the cDNA sequence for a known gene.  
SEQ ID NO:457 is the cDNA sequence for a known gene.  
SEQ ID NO:458 is the cDNA sequence for a previously identified gene.  
SEQ ID NO:459 is the cDNA sequence for 23045.  
SEQ ID NO:460 is the cDNA sequence for 23032.  
SEQ ID NO:461 is the cDNA sequence for 23054.  
SEQ ID NOs:462-467 are cDNA sequences for known genes.  
SEQ ID NOs:468-471 are cDNA sequences for P710P.  
SEQ ID NO:472 is a cDNA sequence for P1001C.

#### DETAILED DESCRIPTION OF THE INVENTION

As noted above, the present invention is generally directed to compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer. The compositions described herein may include prostate tumor polypeptides, polynucleotides encoding such polypeptides, binding agents such as antibodies, antigen presenting cells (APCs) and/or immune system cells (e.g., T cells). Polypeptides of the present invention generally comprise at least a portion (such as an immunogenic portion) of a prostate tumor protein or a variant thereof. A "prostate tumor protein" is a protein that is expressed in prostate tumor cells at a level that is at least two fold, and preferably at least five fold, greater than the level of expression in a normal tissue, as determined using a representative assay provided herein. Certain prostate tumor proteins are tumor proteins that react detectably (within an immunoassay, such as an ELISA or Western blot) with antisera of a patient afflicted with prostate cancer. Polynucleotides of the subject invention generally comprise a DNA or RNA sequence that encodes all or a portion of such a polypeptide, or that is complementary to such a sequence. Antibodies are generally immune system proteins, or antigen-binding fragments thereof, that are capable of binding to a polypeptide as described above. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B-cells that express a polypeptide as described above. T cells that may be employed within such compositions are generally T cells that are specific for a polypeptide as described above.



The present invention is based on the discovery of human prostate tumor proteins. Sequences of polynucleotides encoding certain tumor proteins, or portions thereof, are provided in SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472. Sequences of polypeptides comprising at least a portion of a tumor protein are provided in SEQ ID NOs:112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380 and 383.

#### PROSTATE TUMOR PROTEIN POLYNUCLEOTIDES

Any polynucleotide that encodes a prostate tumor protein or a portion or other variant thereof as described herein is encompassed by the present invention. Preferred polynucleotides comprise at least 15 consecutive nucleotides, preferably at least 30 consecutive nucleotides and more preferably at least 45 consecutive nucleotides, that encode a portion of a prostate tumor protein. More preferably, a polynucleotide encodes an immunogenic portion of a prostate tumor protein. Polynucleotides complementary to any such sequences are also encompassed by the present invention. Polynucleotides may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules include HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the present invention, and a polynucleotide may, but need not, be linked to other molecules and/or support materials.

Polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a prostate tumor protein or a portion thereof) or may comprise a variant of such a sequence. Polynucleotide variants may contain one or more substitutions, additions, deletions and/or insertions such that the immunogenicity of the encoded polypeptide is not diminished, relative to a native tumor protein. The effect on the immunogenicity of the encoded polypeptide may generally be assessed as described herein. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native prostate tumor protein or a portion thereof.

Two polynucleotide or polypeptide sequences are said to be "identical" if the sequence of nucleotides or amino acids in the two sequences is the same when aligned for maximum correspondence as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50,

in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) *Atlas of Protein Sequence and Structure*, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenesis pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad. Sci. USA* 80:726-730.

Preferably, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide or polypeptide sequence in the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.*, the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

Variants may also, or alternatively, be substantially homologous to a native gene, or a portion or complement thereof. Such polynucleotide variants are capable of hybridizing under moderately stringent conditions to a naturally occurring DNA sequence encoding a native prostate tumor protein (or a complementary sequence). Suitable moderately stringent conditions include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5 X SSC, overnight; followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS.

It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to

the nucleotide sequence of any native gene. Nonetheless, polynucleotides that vary due to differences in codon usage are specifically contemplated by the present invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

Polynucleotides may be prepared using any of a variety of techniques. For example, a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (*i.e.*, expression that is at least five fold greater in a prostate tumor than in normal tissue, as determined using a representative assay provided herein). Such screens may be performed using a Synteni microarray (Palo Alto, CA) according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Alternatively, polypeptides may be amplified from cDNA prepared from cells expressing the proteins described herein, such as prostate tumor cells. Such polynucleotides may be amplified via polymerase chain reaction (PCR). For this approach, sequence-specific primers may be designed based on the sequences provided herein, and may be purchased or synthesized.

An amplified portion may be used to isolate a full length gene from a suitable library (*e.g.*, a prostate tumor cDNA library) using well known techniques. Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide probes or primers suitable for amplification. Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be preferred for identifying 5' and upstream regions of genes. Genomic libraries are preferred for obtaining introns and extending 5' sequences.

For hybridization techniques, a partial sequence may be labeled (*e.g.*, by nick-translation or end-labeling with  $^{32}\text{P}$ ) using well known techniques. A bacterial or bacteriophage library is then screened by hybridizing filters containing denatured bacterial colonies (or lawns containing phage plaques) with the labeled probe (*see* Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may be analyzed to determine the amount of additional sequence by, for example, PCR using a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The complete sequence may then be determined using

standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences are then assembled into a single contiguous sequence. A full length cDNA molecule can be generated by ligating suitable fragments, using well known techniques.

Alternatively, there are numerous amplification techniques for obtaining a full length coding sequence from a partial cDNA sequence. Within such techniques, amplification is generally performed via PCR. Any of a variety of commercially available kits may be used to perform the amplification step. Primers may be designed using, for example, software well known in the art. Primers are preferably 22-30 nucleotides in length, have a GC content of at least 50% and anneal to the target sequence at temperatures of about 68°C to 72°C. The amplified region may be sequenced as described above, and overlapping sequences assembled into a contiguous sequence.

One such amplification technique is inverse PCR (*see* Triglia et al., *Nucl. Acids Res.* 16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be retrieved by amplification with a primer to a linker sequence and a primer specific to a known region. The amplified sequences are typically subjected to a second round of amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO 96/38591. Another such technique is known as "rapid amplification of cDNA ends" or RACE. This technique involves the use of an internal primer and an external primer, which hybridizes to a polyA region or vector sequence, to identify sequences that are 5' and 3' of a known sequence. Additional techniques include capture PCR (Lagerstrom et al., *PCR Methods Applic.* 1:111-19, 1991) and walking PCR (Parker et al., *Nucl. Acids. Res.* 19:3055-60, 1991). Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed using well known programs (*e.g.*, NCBI BLAST searches), and such ESTs may be used to generate a contiguous full length sequence.

Certain nucleic acid sequences of cDNA molecules encoding at least a portion of a prostate tumor protein are provided in SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472. Isolation of these

polynucleotides is described below. Each of these prostate tumor proteins was overexpressed in prostate tumor tissue.

Polynucleotide variants may generally be prepared by any method known in the art, including chemical synthesis by, for example, solid phase phosphoramidite chemical synthesis. Modifications in a polynucleotide sequence may also be introduced using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis (see Adelman et al., *DNA* 2:183, 1983). Alternatively, RNA molecules may be generated by *in vitro* or *in vivo* transcription of DNA sequences encoding a prostate tumor protein, or portion thereof, provided that the DNA is incorporated into a vector with a suitable RNA polymerase promoter (such as T7 or SP6). Certain portions may be used to prepare an encoded polypeptide, as described herein. In addition, or alternatively, a portion may be administered to a patient such that the encoded polypeptide is generated *in vivo* (e.g., by transfecting antigen-presenting cells, such as dendritic cells, with a cDNA construct encoding a prostate tumor polypeptide, and administering the transfected cells to the patient).

A portion of a sequence complementary to a coding sequence (i.e., an antisense polynucleotide) may also be used as a probe or to modulate gene expression. cDNA constructs that can be transcribed into antisense RNA may also be introduced into cells of tissues to facilitate the production of antisense RNA. An antisense polynucleotide may be used, as described herein, to inhibit expression of a tumor protein. Antisense technology can be used to control gene expression through triple-helix formation, which compromises the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors or regulatory molecules (see Gee et al., *In Huber and Carr, Molecular and Immunologic Approaches*, Futura Publishing Co. (Mt. Kisco, NY; 1994)). Alternatively, an antisense molecule may be designed to hybridize with a control region of a gene (e.g., promoter, enhancer or transcription initiation site), and block transcription of the gene; or to block translation by inhibiting binding of a transcript to ribosomes.

A portion of a coding sequence, or of a complementary sequence, may also be designed as a probe or primer to detect gene expression. Probes may be labeled with a variety of reporter groups, such as radionuclides and enzymes, and are preferably at least 10 nucleotides in length, more preferably at least 20 nucleotides in length and still more preferably at least 30 nucleotides in length. Primers, as noted above, are preferably 22-30 nucleotides in length.

Any polynucleotide may be further modified to increase stability *in vivo*. Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3' ends; the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages in the backbone; and/or the inclusion of nontraditional bases such

as inosine, queosine and wybutosine, as well as acetyl- methyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

Nucleotide sequences as described herein may be joined to a variety of other nucleotide sequences using established recombinant DNA techniques. For example, a polynucleotide may be cloned into any of a variety of cloning vectors, including plasmids, phagemids, lambda phage derivatives and cosmids. Vectors of particular interest include expression vectors, replication vectors, probe generation vectors and sequencing vectors. In general, a vector will contain an origin of replication functional in at least one organism, convenient restriction endonuclease sites and one or more selectable markers. Other elements will depend upon the desired use, and will be apparent to those of ordinary skill in the art.

Within certain embodiments, polynucleotides may be formulated so as to permit entry into a cell of a mammal, and expression therein. Such formulations are particularly useful for therapeutic purposes, as described below. Those of ordinary skill in the art will appreciate that there are many ways to achieve expression of a polynucleotide in a target cell, and any suitable method may be employed. For example, a polynucleotide may be incorporated into a viral vector such as, but not limited to, adenovirus, adeno-associated virus, retrovirus, or vaccinia or other pox virus (*e.g.*, avian pox virus). Techniques for incorporating DNA into such vectors are well known to those of ordinary skill in the art. A retroviral vector may additionally transfer or incorporate a gene for a selectable marker (to aid in the identification or selection of transduced cells) and/or a targeting moiety, such as a gene that encodes a ligand for a receptor on a specific target cell, to render the vector target specific. Targeting may also be accomplished using an antibody, by methods known to those of ordinary skill in the art.

Other formulations for therapeutic purposes include colloidal dispersion systems, such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes. A preferred colloidal system for use as a delivery vehicle *in vitro* and *in vivo* is a liposome (*i.e.*, an artificial membrane vesicle). The preparation and use of such systems is well known in the art.

#### PROSTATE TUMOR POLYPEPTIDES

Within the context of the present invention, polypeptides may comprise at least an immunogenic portion of a prostate tumor protein or a variant thereof, as described herein. As noted above, a "prostate tumor protein" is a protein that is expressed by prostate tumor cells. Proteins that are prostate tumor proteins also react detectably within an immunoassay (such as an ELISA) with antisera from a patient with prostate cancer. Polypeptides as described herein may be of any length. Additional sequences derived from

the native protein and/or heterologous sequences may be present, and such sequences may (but need not) possess further immunogenic or antigenic properties.

An "immunogenic portion," as used herein is a portion of a protein that is recognized (*i.e.*, specifically bound) by a B-cell and/or T-cell surface antigen receptor. Such immunogenic portions generally comprise at least 5 amino acid residues, more preferably at least 10, and still more preferably at least 20 amino acid residues of a prostate tumor protein or a variant thereof. Certain preferred immunogenic portions include peptides in which an N-terminal leader sequence and/or transmembrane domain have been deleted. Other preferred immunogenic portions may contain a small N- and/or C-terminal deletion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids), relative to the mature protein.

Immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, *Fundamental Immunology*, 3rd ed., 243-247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides for the ability to react with antigen-specific antibodies, antisera and/or T-cell lines or clones. As used herein, antisera and antibodies are "antigen-specific" if they specifically bind to an antigen (*i.e.*, they react with the protein in an ELISA or other immunoassay, and do not react detectably with unrelated proteins). Such antisera and antibodies may be prepared as described herein, and using well known techniques. An immunogenic portion of a native prostate tumor protein is a portion that reacts with such antisera and/or T-cells at a level that is not substantially less than the reactivity of the full length polypeptide (*e.g.*, in an ELISA and/or T-cell reactivity assay). Such immunogenic portions may react within such assays at a level that is similar to or greater than the reactivity of the full length polypeptide. Such screens may generally be performed using methods well known to those of ordinary skill in the art, such as those described in Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. For example, a polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the sera to the immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, <sup>125</sup>I-labeled Protein A.

As noted above, a composition may comprise a variant of a native prostate tumor protein. A polypeptide "variant," as used herein, is a polypeptide that differs from a native prostate tumor protein in one or more substitutions, deletions, additions and/or insertions, such that the immunogenicity of the polypeptide is not substantially diminished. In other words, the ability of a variant to react with antigen-specific antisera may be enhanced or unchanged, relative to the native protein, or may be diminished by less than 50%, and preferably less than 20%, relative to the native protein. Such variants may generally be identified by modifying one of the above polypeptide sequences and evaluating the reactivity of the modified polypeptide with antigen-specific antibodies or antisera as described herein.

Preferred variants include those in which one or more portions, such as an N-terminal leader sequence or transmembrane domain, have been removed. Other preferred variants include variants in which a small portion (e.g., 1-30 amino acids, preferably 5-15 amino acids) has been removed from the N- and/or C-terminal of the mature protein. Polypeptide variants preferably exhibit at least about 70%, more preferably at least about 90% and most preferably at least about 95% identity (determined as described above) to the identified polypeptides.

Preferably, a variant contains conservative substitutions. A "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydrophobic nature of the polypeptide to be substantially unchanged. Amino acid substitutions may generally be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity values include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain nonconservative changes. In a preferred embodiment, variant polypeptides differ from a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino acids that have minimal influence on the immunogenicity, secondary structure and hydrophobic nature of the polypeptide.

As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (e.g., poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

Polypeptides may be prepared using any of a variety of well known techniques. Recombinant polypeptides encoded by DNA sequences as described above may be readily prepared from the DNA sequences using any of a variety of expression vectors known to those of ordinary skill in the art. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a DNA molecule that encodes a recombinant polypeptide. Suitable host cells include prokaryotes, yeast and higher eukaryotic cells. Preferably, the host cells employed are



*E. coli*, yeast or a mammalian cell line such as COS or CHO. Supernatants from suitable host/vector systems which secrete recombinant protein or polypeptide into culture media may be first concentrated using a commercially available filter. Following concentration, the concentrate may be applied to a suitable purification matrix such as an affinity matrix or an ion exchange resin. Finally, one or more reverse phase HPLC steps can be employed to further purify a recombinant polypeptide.

Portions and other variants having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may also be generated by synthetic means, using techniques well known to those of ordinary skill in the art. For example, such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. See Merrifield, *J. Am. Chem. Soc.* 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems Division (Foster City, CA), and may be operated according to the manufacturer's instructions.

Within certain specific embodiments, a polypeptide may be a fusion protein that comprises multiple polypeptides as described herein, or that comprises at least one polypeptide as described herein and an unrelated sequence, such as a known tumor protein. A fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner), preferably T helper epitopes recognized by humans, or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing fusion partners. Other fusion partners may be selected so as to increase the solubility of the protein or to enable the protein to be targeted to desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the protein.

Fusion proteins may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion protein is expressed as a recombinant protein, allowing the production of increased levels, relative to a non-fused protein, in an expression system. Briefly, DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that the reading frames of the sequences are in phase. This permits translation into a single fusion protein that retains the biological activity of both component polypeptides.

A peptide linker sequence may be employed to separate the first and the second polypeptide components by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into

the fusion protein using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., *Gene* 40:39-46, 1985; Murphy et al., *Proc. Natl. Acad. Sci. USA* 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and second polypeptides have non-essential N-terminal amino acid regions that can be used to separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

Fusion proteins are also provided that comprise a polypeptide of the present invention together with an unrelated immunogenic protein. Preferably the immunogenic protein is capable of eliciting a recall response. Examples of such proteins include tetanus, tuberculosis and hepatitis proteins (*see*, for example, Stoute et al. *New Engl. J. Med.*, 336:86-91, 1997).

Within preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium *Haemophilus influenza B* (WO 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (*e.g.*, the first N-terminal 100-110 amino acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in *E. coli* (thus functioning as an expression enhancer). The lipid tail ensures optimal presentation of the antigen to antigen presenting cells. Other fusion partners include the non-structural protein from influenzae virus, NS1 (hemagglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

In another embodiment, the immunological fusion partner is the protein known as LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is derived from *Streptococcus pneumoniae*, which synthesizes an N-acetyl-L-alanine amidase known as

amidase LYTA (encoded by the *LytA* gene; *Gene* 43:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of the LYTA protein is responsible for the affinity to the choline or to some choline analogues such as DEAE. This property has been exploited for the development of *E. coli* C-LYTA expressing plasmids useful for expression of fusion proteins. Purification of hybrid proteins containing the C-LYTA fragment at the amino terminus has been described (see *Biotechnology* 10:795-798, 1992). Within a preferred embodiment, a repeat portion of LYTA may be incorporated into a fusion protein. A repeat portion is found in the C-terminal region starting at residue 178. A particularly preferred repeat portion incorporates residues 188-305.

In general, polypeptides (including fusion proteins) and polynucleotides as described herein are isolated. An "isolated" polypeptide or polynucleotide is one that is removed from its original environment. For example, a naturally-occurring protein is isolated if it is separated from some or all of the coexisting materials in the natural system. Preferably, such polypeptides are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99% pure. A polynucleotide is considered to be isolated if, for example, it is cloned into a vector that is not a part of the natural environment.

#### BINDING AGENTS

The present invention further provides agents, such as antibodies and antigen-binding fragments thereof, that specifically bind to a prostate tumor protein. As used herein, an antibody, or antigen-binding fragment thereof, is said to "specifically bind" to a prostate tumor protein if it reacts at a detectable level (within, for example, an ELISA) with a prostate tumor protein, and does not react detectably with unrelated proteins under similar conditions. As used herein, "binding" refers to a noncovalent association between two separate molecules such that a complex is formed. The ability to bind may be evaluated by, for example, determining a binding constant for the formation of the complex. The binding constant is the value obtained when the concentration of the complex is divided by the product of the component concentrations. In general, two compounds are said to "bind," in the context of the present invention, when the binding constant for complex formation exceeds about  $10^3$  L/mol. The binding constant may be determined using methods well known in the art.

Binding agents may be further capable of differentiating between patients with and without a cancer, such as prostate cancer, using the representative assays provided herein. In other words, antibodies or other binding agents that bind to a prostate tumor protein will generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, and will generate a negative signal indicating the absence of the disease in at least about 90% of individuals without the cancer. To determine whether a binding agent satisfies this requirement, biological samples (*e.g.*, blood, sera, urine and/or tumor biopsies) from

patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. It will be apparent that a statistically significant number of samples with and without the disease should be assayed. Each binding agent should satisfy the above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent. For example, a binding agent may be a ribosome, with or without a peptide component, an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. See, e.g., Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (e.g., mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically. Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for an antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. Immunol.* 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (i.e., reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient

time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

Within certain embodiments, the use of antigen-binding fragments of antibodies may be preferred. Such fragments include Fab fragments, which may be prepared using standard techniques. Briefly, immunoglobulins may be purified from rabbit serum by affinity chromatography on Protein A bead columns (Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988) and digested by papain to yield Fab and Fc fragments. The Fab and Fc fragments may be separated by affinity chromatography on protein A bead columns.

Monoclonal antibodies of the present invention may be coupled to one or more therapeutic agents. Suitable agents in this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include  $^{90}\text{Y}$ ,  $^{125}\text{I}$ ,  $^{125}\text{I}$ ,  $^{131}\text{I}$ ,  $^{186}\text{Re}$ ,  $^{188}\text{Re}$ ,  $^{211}\text{At}$ , and  $^{212}\text{Bi}$ . Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred toxins include ricin, abrin, diphtheria toxin, cholera toxin, gelonin, Pseudomonas exotoxin, Shigella toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (*e.g.*, covalently bonded) to a suitable monoclonal antibody either directly or indirectly (*e.g.*, via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid halide, or with an alkyl group containing a good leaving group (*e.g.*, a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and

thus increase the coupling efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents, which otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be effected, for example, through amino groups, carboxyl groups, sulfhydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, *e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is cleavable during or upon internalization into a cell. A number of different cleavable linker groups have been described. The mechanisms for the intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (*e.g.*, U.S. Patent No. 4,489,710, to Spitler), by irradiation of a photolabile bond (*e.g.*, U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of derivatized amino acid side chains (*e.g.*, U.S. Patent No. 4,638,045, to Kohn et al.), by serum complement-mediated hydrolysis (*e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (*e.g.*, U.S. Patent No. 4,569,789, to Blattler et al.).

It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody. Regardless of the particular embodiment, immunoconjugates with more than one agent may be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or linkers which provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

A carrier may bear the agents in a variety of ways, including covalent bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (*e.g.*, U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (*e.g.*, U.S. Patent No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (*e.g.*, U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

A variety of routes of administration for the antibodies and immunoconjugates may be used. Typically, administration will be intravenous, intramuscular, subcutaneous or in the bed of a resected tumor. It will be evident that the precise dose of the antibody/immunoconjugate will vary depending upon the antibody used, the antigen density on the tumor, and the rate of clearance of the antibody.

#### T CELLS

Immunotherapeutic compositions may also, or alternatively, comprise T cells specific for a prostate tumor protein. Such cells may generally be prepared *in vitro* or *ex vivo*, using standard procedures. For example, T cells may be isolated from bone marrow, peripheral blood, or a fraction of bone marrow or peripheral blood of a patient, using a commercially available cell separation system, such as the CEPRATE™ system, available from CellPro Inc., Bothell WA (see also U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243). Alternatively, T cells may be derived from related or unrelated humans, non-human mammals, cell lines or cultures.

T cells may be stimulated with a prostate tumor polypeptide, polynucleotide encoding a prostate tumor polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the polypeptide. Preferably, a prostate tumor polypeptide or polynucleotide is present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

T cells are considered to be specific for a prostate tumor polypeptide if the T cells kill target cells coated with the polypeptide or expressing a gene encoding the polypeptide. T cell specificity may be evaluated using any of a variety of standard techniques. For example, within a chromium release assay or proliferation assay, a stimulation index of more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen et al., *Cancer Res.* 54:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be accomplished by a variety of known techniques. For example, T cell proliferation can be detected by measuring an increased rate of DNA synthesis (e.g., by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a prostate tumor polypeptide (100 ng/ml - 100 µg/ml, preferably 200 ng/ml - 25 µg/ml) for 3 - 7 days should result in at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in activation of the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (e.g., TNF or IFN-γ) is indicative of T cell activation (see Coligan et al., *Current Protocols in Immunology*, vol. 1, Wiley Interscience

(Greene 1998)). T cells that have been activated in response to a prostate tumor polypeptide, polynucleotide or polypeptide-expressing APC may be CD4<sup>+</sup> and/or CD8<sup>+</sup>. Prostate tumor protein-specific T cells may be expanded using standard techniques. Within preferred embodiments, the T cells are derived from either a patient or a related, or unrelated, donor and are administered to the patient following stimulation and expansion.

For therapeutic purposes, CD4<sup>+</sup> or CD8<sup>+</sup> T cells that proliferate in response to a prostate tumor polypeptide, polynucleotide or APC can be expanded in number either *in vitro* or *in vivo*. Proliferation of such T cells *in vitro* may be accomplished in a variety of ways. For example, the T cells can be re-exposed to a prostate tumor polypeptide, or a short peptide corresponding to an immunogenic portion of such a polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator cells that synthesize a prostate tumor polypeptide. Alternatively, one or more T cells that proliferate in the presence of a prostate tumor protein can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution.

#### PHARMACEUTICAL COMPOSITIONS AND VACCINES

Within certain aspects, polypeptides, polynucleotides, T cells and/or binding agents disclosed herein may be incorporated into pharmaceutical compositions or immunogenic compositions (*i.e.*, vaccines). Pharmaceutical compositions comprise one or more such compounds and a physiologically acceptable carrier. Vaccines may comprise one or more such compounds and a non-specific immune response enhancer. A non-specific immune response enhancer may be any substance that enhances an immune response to an exogenous antigen. Examples of non-specific immune response enhancers include adjuvants, biodegradable microspheres (*e.g.*, polylactic galactide) and liposomes (into which the compound is incorporated; *see e.g.*, Fullerton, U.S. Patent No. 4,235,877). Vaccine preparation is generally described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Pharmaceutical compositions and vaccines within the scope of the present invention may also contain other compounds, which may be biologically active or inactive. For example, one or more immunogenic portions of other tumor antigens may be present, either incorporated into a fusion polypeptide or as a separate compound, within the composition or vaccine.

A pharmaceutical composition or vaccine may contain DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated *in situ*. As noted above, the DNA may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, bacteria and viral expression systems. Numerous gene delivery techniques are well known in the art, such as those described by Rolland, *Crit. Rev. Therap. Drug Carrier Systems* 15:143-198, 1998,



and references cited therein. Appropriate nucleic acid expression systems contain the necessary DNA sequences for expression in the patient (such as a suitable promoter and terminating signal). Bacterial delivery systems involve the administration of a bacterium (such as *Bacillus-Calmette-Guerrin*) that expresses an immunogenic portion of the polypeptide on its cell surface or secretes such an epitope. In a preferred embodiment, the DNA may be introduced using a viral expression system (e.g., vaccinia or other pox virus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic (defective), replication competent virus. Suitable systems are disclosed, for example, in Fisher-Hoch et al., *Proc. Natl. Acad. Sci. USA* 86:317-321, 1989; Flexner et al., *Ann. N.Y. Acad. Sci.* 569:86-103, 1989; Flexner et al., *Vaccine* 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; WO 91/02805; Berkner, *Biotechniques* 6:616-627, 1988; Rosenfeld et al., *Science* 252:431-434, 1991; Kolls et al., *Proc. Natl. Acad. Sci. USA* 91:215-219, 1994; Kass-Eisler et al., *Proc. Natl. Acad. Sci. USA* 90:11498-11502, 1993; Guzman et al., *Circulation* 88:2838-2848, 1993; and Guzman et al., *Cir. Res.* 73:1202-1207, 1993. Techniques for incorporating DNA into such expression systems are well known to those of ordinary skill in the art. The DNA may also be "naked," as described, for example, in Ulmer et al., *Science* 259:1745-1749, 1993 and reviewed by Cohen, *Science* 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary depending on the mode of administration. Compositions of the present invention may be formulated for any appropriate manner of administration, including for example, topical, oral, nasal, intravenous, intracranial, intraperitoneal, subcutaneous or intramuscular administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a fat, a wax or a buffer. For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (e.g., polylactate polyglycolate) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268 and 5,075,109.

Such compositions may also comprise buffers (e.g., neutral buffered saline or phosphate buffered saline), carbohydrates (e.g., glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, chelating agents such as EDTA or glutathione, adjuvants (e.g., aluminum hydroxide) and/or

preservatives. Alternatively, compositions of the present invention may be formulated as a lyophilizate. Compounds may also be encapsulated within liposomes using well known technology.

Any of a variety of non-specific immune response enhancers may be employed in the vaccines of this invention. For example, an adjuvant may be included. Most adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, *Bordetella pertussis* or *Mycobacterium tuberculosis* derived proteins. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF or interleukin-2, -7, or -12, may also be used as adjuvants.

Within the vaccines provided herein, the adjuvant composition is preferably designed to induce an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (e.g., IFN- $\gamma$ , IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (e.g., IL-4, IL-5, IL-6, IL-10 and TNF- $\beta$ ) tend to favor the induction of humoral immune responses. Following application of a vaccine as provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using standard assays. For a review of the families of cytokines, see Mosmann and Coffman, *Ann. Rev. Immunol.* 7:145-173, 1989.

Preferred adjuvants for use in eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A (3D-MPL), together with an aluminum salt. MPL adjuvants are available from Ribi ImmunoChem Research Inc. (Hamilton, MT; see US Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555. Another preferred adjuvant is a saponin, preferably QS21, which may be used alone or in combination with other adjuvants. For example, an enhanced system involves the combination of a monophosphoryl lipid A and saponin derivative, such as the combination of QS21 and 3D-MPL as described in WO 94/00153, or a less reactogenic composition where the QS21 is

quenched with cholesterol, as described in WO 96/33739. Other preferred formulations comprises an oil-in-water emulsion and tocopherol. A particularly potent adjuvant formulation involving QS21, 3D-MPL and tocopherol in an oil-in-water emulsion is described in WO 95/17210. Any vaccine provided herein may be prepared using well known methods that result in a combination of antigen, immune response enhancer and a suitable carrier or excipient.

The compositions described herein may be administered as part of a sustained release formulation (*i.e.*, a formulation such as a capsule or sponge that effects a slow release of compound following administration). Such formulations may generally be prepared using well known technology and administered by, for example, oral, rectal or subcutaneous implantation, or by implantation at the desired target site. Sustained-release formulations may contain a polypeptide, polynucleotide or antibody dispersed in a carrier matrix and/or contained within a reservoir surrounded by a rate controlling membrane. Carriers for use within such formulations are biocompatible, and may also be biodegradable; preferably the formulation provides a relatively constant level of active component release. The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

Any of a variety of delivery vehicles may be employed within pharmaceutical compositions and vaccines to facilitate production of an antigen-specific immune response that targets tumor cells. Delivery vehicles include antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the antigen, to improve activation and/or maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

Certain preferred embodiments of the present invention use dendritic cells or progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature* 392:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (see Timmerman and Levy, *Ann. Rev. Med.* 50:507-529, 1999). In general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*) and based on the lack of differentiation markers of B cells (CD19 and CD20), T cells (CD3), monocytes (CD14) and natural killer cells (CD56), as determined using standard assays. Dendritic cells may, of course, be engineered to express specific cell-

surface receptors or ligands that are not commonly found on dendritic cells *in vivo* or *ex vivo*, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (see Zitvogel et al., *Nature Med.* 4:594-600, 1998).

Dendritic cells and progenitors may be obtained from peripheral blood, bone marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNF $\alpha$  to cultures of monocytes harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNF $\alpha$ , CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce maturation and proliferation of dendritic cells.

Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which correlates with the high expression of Fc $\gamma$  receptor, mannose receptor and DEC-205 marker. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II MHC, adhesion molecules (e.g., CD54 and CD11) and costimulatory molecules (e.g., CD40, CD80 and CD86).

APCs may generally be transfected with a polynucleotide encoding a prostate tumor protein (or portion or other variant thereof) such that the prostate tumor polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place *ex vivo*, and a composition or vaccine comprising such transfected cells may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection that occurs *in vivo*. *In vivo* and *ex vivo* transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., *Immunology and cell Biology* 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or progenitor cells with the prostate tumor polypeptide, DNA (naked or within a plasmid vector) or RNA; or with antigen-expressing recombinant bacterium or viruses (e.g., vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that

provides T cell help (e.g., a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated immunological partner, separately or in the presence of the polypeptide.

#### CANCER THERAPY

In further aspects of the present invention, the compositions described herein may be used for immunotherapy of cancer, such as prostate cancer. Within such methods, pharmaceutical compositions and vaccines are typically administered to a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human. A patient may or may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions and vaccines may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. A cancer may be diagnosed using criteria generally accepted in the art, including the presence of a malignant tumor. Pharmaceutical compositions and vaccines may be administered either prior to or following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous host immune system to react against tumors with the administration of immune response-modifying agents (such as polypeptides and polynucleotides disclosed herein).

Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not necessarily depend on an intact host immune system. Examples of effector cells include T cells as discussed above, T lymphocytes (such as CD8<sup>+</sup> cytotoxic T lymphocytes and CD4<sup>+</sup> T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody receptors specific for the polypeptides recited herein may be cloned, expressed and transferred into other vectors or effector cells for adoptive immunotherapy. The polypeptides provided herein may also be used to generate antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth *in vitro*, as described herein. Culture conditions for expanding single antigen-specific effector cells to several billion in number with retention of antigen recognition *in vivo* are well known in the art. Such *in vitro* culture conditions typically use intermittent stimulation with antigen, often in the presence of cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein

may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage, monocyte, fibroblast or B cells, may be pulsed with immunoreactive polypeptides or transfected with one or more polynucleotides using standard techniques well known in the art. For example, antigen-presenting cells can be transfected with a polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term *in vivo*. Studies have shown that cultured effector cells can be induced to grow *in vivo* and to survive long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (*see, for example, Cheever et al., Immunological Reviews 157:177, 1997*).

Alternatively, a vector expressing a polypeptide recited herein may be introduced into antigen presenting cells taken from a patient and clonally propagated *ex vivo* for transplant back into the same patient. Transfected cells may be reintroduced into the patient using any means known in the art, preferably in sterile form by intravenous, intracavitary, intraperitoneal or intratumor administration.

Routes and frequency of administration of the therapeutic compositions disclosed herein, as well as dosage, will vary from individual to individual, and may be readily established using standard techniques. In general, the pharmaceutical compositions and vaccines may be administered by injection (*e.g.*, intracutaneous, intramuscular, intravenous or subcutaneous), intranasally (*e.g.*, by aspiration) or orally. Preferably, between 1 and 10 doses may be administered over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50% above the basal (*i.e.*, untreated) level. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells *in vitro*. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to non-vaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 100 µg to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such

a response can be monitored by establishing an improved clinical outcome (e.g., more frequent remissions, complete or partial, or longer disease-free survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to a prostate tumor protein generally correlate with an improved clinical outcome. Such immune responses may generally be evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples obtained from a patient before and after treatment.

#### METHODS FOR DETECTING CANCER

In general, a cancer may be detected in a patient based on the presence of one or more prostate tumor proteins and/or polynucleotides encoding such proteins in a biological sample (for example, blood, sera, urine and/or tumor biopsies) obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as prostate cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided herein generally permit detection of the level of antigen that binds to the agent in the biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer. In general, a prostate tumor sequence should be present at a level that is at least three fold higher in tumor tissue than in normal tissue

There are a variety of assay formats known to those of ordinary skill in the art for using a binding agent to detect polypeptide markers in a sample. See, e.g., Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c) comparing the level of polypeptide with a predetermined cut-off value.

In a preferred embodiment, the assay involves the use of binding agent immobilized on a solid support to bind to and remove the polypeptide from the remainder of the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding agent/polypeptide complex. Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G, protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding

agent. Suitable polypeptides for use within such assays include full length prostate tumor proteins and portions thereof to which the binding agent binds, as described above.

The solid support may be any material known to those of ordinary skill in the art to which the tumor protein may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of binding agent ranging from about 10 ng to about 10  $\mu$ g, and preferably about 100 ng to about 1  $\mu$ g, is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (*see, e.g.,* Pierce Immunotechnology Catalog and Handbook, 1991, at A12-A13).

In certain embodiments, the assay is a two-antibody sandwich assay. This assay may be performed by first contacting an antibody that has been immobilized on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody. Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a detection reagent (preferably a second antibody capable of binding to a different site on the polypeptide) containing a reporter group is added. The amount of detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.



More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 20™ (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.*, incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with prostate cancer. Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20™. The second antibody, which contains a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

The detection reagent is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide. An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of time. Unbound detection reagent is then removed and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products.

To determine the presence or absence of a cancer, such as prostate cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is the average mean signal obtained when the immobilized antibody is incubated with samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred

embodiment, the cut-off value is determined using a Receiver Operator Curve, according to the method of Sackett et al., *Clinical Epidemiology: A Basic Science for Clinical Medicine*, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (i.e., sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (i.e., the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered positive. Alternatively, the cut-off value may be shifted to the left along the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, labeled binding agent then binds to the binding agent-polypeptide complex as a solution containing the second binding agent flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent. Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1  $\mu$ g, and more preferably from about 50 ng to about 500 ng. Such tests can typically be performed with a very small amount of biological sample.

Of course, numerous other assay protocols exist that are suitable for use with the tumor proteins or binding agents of the present invention. The above descriptions are intended to be exemplary only. For example, it will be apparent to those of ordinary skill in the art that the above protocols may be readily modified to use prostate tumor polypeptides to

detect antibodies that bind to such polypeptides in a biological sample. The detection of such prostate tumor protein specific antibodies may correlate with the presence of a cancer.

A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with a prostate tumor protein in a biological sample. Within certain methods, a biological sample comprising CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient is incubated with a prostate tumor polypeptide, a polynucleotide encoding such a polypeptide and/or an APC that expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells. For example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may be incubated *in vitro* for 2-9 days (typically 4 days) at 37°C with prostate tumor polypeptide (e.g., 5 - 25 µg/ml). It may be desirable to incubate another aliquot of a T cell sample in the absence of prostate tumor polypeptide to serve as a control. For CD4<sup>+</sup> T cells, activation is preferably detected by evaluating proliferation of the T cells. For CD8<sup>+</sup> T cells, activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

As noted above, a cancer may also, or alternatively, be detected based on the level of mRNA encoding a prostate tumor protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to amplify a portion of a prostate tumor cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (i.e., hybridizes to) a polynucleotide encoding the prostate tumor protein. The amplified cDNA is then separated and detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding a prostate tumor protein may be used in a hybridization assay to detect the presence of polynucleotide encoding the tumor protein in a biological sample.

To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%, preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding a prostate tumor protein that is at least 10 nucleotides, and preferably at least 20 nucleotides, in length. Preferably, oligonucleotide primers and/or probes will hybridize to a polynucleotide encoding a polypeptide disclosed herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers

comprise at least 10 contiguous nucleotides, more preferably at least 15 contiguous nucleotides, of a DNA molecule having a sequence recited in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375 and 381. Techniques for both PCR based assays and hybridization assays are well known in the art (see, for example, Mullis et al., *Cold Spring Harbor Symp. Quant. Biol.*, 51:263, 1987; Erlich ed., *PCR Technology*, Stockton Press, NY, 1989).

One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, such as biopsy tissue, and is reverse transcribed to produce cDNA molecules. PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification may be performed on biological samples taken from a test patient and from an individual who is not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered positive.

In another embodiment, the disclosed compositions may be used as markers for the progression of cancer. In this embodiment, assays as described above for the diagnosis of a cancer may be performed over time, and the change in the level of reactive polypeptide(s) or polynucleotide evaluated. For example, the assays may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In general, a cancer is progressing in those patients in whom the level of polypeptide or polynucleotide detected increases over time. In contrast, the cancer is not progressing when the level of reactive polypeptide or polynucleotide either remains constant or decreases with time.

Certain *in vivo* diagnostic assays may be performed directly on a tumor. One such assay involves contacting tumor cells with a binding agent. The bound binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may also be used in histological applications. Alternatively, polynucleotide probes may be used within such applications.

As noted above, to improve sensitivity, multiple prostate tumor protein markers may be assayed within a given sample. It will be apparent that binding agents specific for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of tumor protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or alternatively, assays for tumor proteins provided herein may be combined with assays for other known tumor antigens.

#### DIAGNOSTIC KITS

The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components necessary for performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For example, one container within a kit may contain a monoclonal antibody or fragment thereof that specifically binds to a prostate tumor protein. Such antibodies or fragments may be provided attached to a support material, as described above. One or more additional containers may enclose elements, such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively, contain a detection reagent as described above that contains a reporter group suitable for direct or indirect detection of antibody binding.

Alternatively, a kit may be designed to detect the level of mRNA encoding a prostate tumor protein in a biological sample. Such kits generally comprise at least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding a prostate tumor protein. Such an oligonucleotide may be used, for example, within a PCR or hybridization assay. Additional components that may be present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding a prostate tumor protein.

The following Examples are offered by way of illustration and not by way of limitation.

## EXAMPLES

### EXAMPLE 1

#### ISOLATION AND CHARACTERIZATION OF PROSTATE TUMOR POLYPEPTIDES

This Example describes the isolation of certain prostate tumor polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library was constructed from prostate tumor poly A<sup>+</sup> RNA using a Superscript Plasmid System for cDNA Synthesis and Plasmid Cloning kit (BRL Life Technologies, Gaithersburg, MD 20897) following the manufacturer's protocol. Specifically, prostate tumor tissues were homogenized with polytron (Kinematica, Switzerland) and total RNA was extracted using Trizol reagent (BRL Life Technologies) as directed by the manufacturer. The poly A<sup>+</sup> RNA was then purified using a Qiagen oligotex spin column mRNA purification kit (Qiagen, Santa Clarita, CA 91355) according to the manufacturer's protocol. First-strand cDNA was synthesized using the NotI/Oligo-dT18 primer. Double-stranded cDNA was synthesized, ligated with EcoRI/BAXI adaptors (Invitrogen, San Diego, CA) and digested with NotI. Following size fractionation with Chroma Spin-1000 columns (Clontech, Palo Alto, CA), the cDNA was ligated into the EcoRI/NotI site of pCDNA3.1 (Invitrogen) and transformed into ElectroMax *E. coli* DH10B cells (BRL Life Technologies) by electroporation.

Using the same procedure, a normal human pancreas cDNA expression library was prepared from a pool of six tissue specimens (Clontech). The cDNA libraries were characterized by determining the number of independent colonies, the percentage of clones that carried insert, the average insert size and by sequence analysis. The prostate tumor library contained  $1.64 \times 10^7$  independent colonies, with 70% of clones having an insert and the average insert size being 1745 base pairs. The normal pancreas cDNA library contained  $3.3 \times 10^6$  independent colonies, with 69% of clones having inserts and the average insert size being 1120 base pairs. For both libraries, sequence analysis showed that the majority of clones had a full length cDNA sequence and were synthesized from mRNA, with minimal rRNA and mitochondrial DNA contamination.

cDNA library subtraction was performed using the above prostate tumor and normal pancreas cDNA libraries, as described by Hara *et al.* (*Blood*, 84:189-199, 1994) with some modifications. Specifically, a prostate tumor-specific subtracted cDNA library was generated as follows. Normal pancreas cDNA library (70 µg) was digested with EcoRI, NotI, and SfuI, followed by a filling-in reaction with DNA polymerase Klenow fragment. After phenol-chloroform extraction and ethanol precipitation, the DNA was dissolved in 100 µl of

H<sub>2</sub>O, heat-denatured and mixed with 100  $\mu$ l (100  $\mu$ g) of Photoprobe biotin (Vector Laboratories, Burlingame, CA). As recommended by the manufacturer, the resulting mixture was irradiated with a 270 W sunlamp on ice for 20 minutes. Additional Photoprobe biotin (50  $\mu$ l) was added and the biotinylation reaction was repeated. After extraction with butanol five times, the DNA was ethanol-precipitated and dissolved in 23  $\mu$ l H<sub>2</sub>O to form the driver DNA.

To form the tracer DNA, 10  $\mu$ g prostate tumor cDNA library was digested with BamHI and XhoI, phenol chloroform extracted and passed through Chroma spin-400 columns (Clontech). Following ethanol precipitation, the tracer DNA was dissolved in 5  $\mu$ l H<sub>2</sub>O. Tracer DNA was mixed with 15  $\mu$ l driver DNA and 20  $\mu$ l of 2 x hybridization buffer (1.5 M NaCl/10 mM EDTA/50 mM HEPES pH 7.5/0.2% sodium dodecyl sulfate), overlaid with mineral oil, and heat-denatured completely. The sample was immediately transferred into a 68 °C water bath and incubated for 20 hours (long hybridization [LH]). The reaction mixture was then subjected to a streptavidin treatment followed by phenol/chloroform extraction. This process was repeated three more times. Subtracted DNA was precipitated, dissolved in 12  $\mu$ l H<sub>2</sub>O, mixed with 8  $\mu$ l driver DNA and 20  $\mu$ l of 2 x hybridization buffer, and subjected to a hybridization at 68 °C for 2 hours (short hybridization [SH]). After removal of biotinylated double-stranded DNA, subtracted cDNA was ligated into BamHI/XhoI site of chloramphenicol resistant pBCSK<sup>+</sup> (Stratagene, La Jolla, CA 92037) and transformed into ElectroMax *E. coli* DH10B cells by electroporation to generate a prostate tumor specific subtracted cDNA library (referred to as "prostate subtraction 1").

To analyze the subtracted cDNA library, plasmid DNA was prepared from 100 independent clones, randomly picked from the subtracted prostate tumor specific library and grouped based on insert size. Representative cDNA clones were further characterized by DNA sequencing with a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A (Foster City, CA). Six cDNA clones, hereinafter referred to as F1-13, F1-12, F1-16, H1-1, H1-9 and H1-4, were shown to be abundant in the subtracted prostate-specific cDNA library. The determined 3' and 5' cDNA sequences for F1-12 are provided in SEQ ID NO: 2 and 3, respectively, with determined 3' cDNA sequences for F1-13, F1-16, H1-1, H1-9 and H1-4 being provided in SEQ ID NO: 1 and 4-7, respectively.

The cDNA sequences for the isolated clones were compared to known sequences in the gene bank using the EMBL and GenBank databases (release 96). Four of the prostate tumor cDNA clones, F1-13, F1-16, H1-1, and H1-4, were determined to encode the following previously identified proteins: prostate specific antigen (PSA), human glandular kallikrein, human tumor expression enhanced gene, and mitochondria cytochrome C oxidase subunit II. H1-9 was found to be identical to a previously identified human

autonomously replicating sequence. No significant homologies to the cDNA sequence for F1-12 were found.

Subsequent studies led to the isolation of a full-length cDNA sequence for F1-12. This sequence is provided in SEQ ID NO: 107, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 108.

To clone less abundant prostate tumor specific genes, cDNA library subtraction was performed by subtracting the prostate tumor cDNA library described above with the normal pancreas cDNA library and with the three most abundant genes in the previously subtracted prostate tumor specific cDNA library: human glandular kallikrein, prostate specific antigen (PSA), and mitochondria cytochrome C oxidase subunit II. Specifically, 1 µg each of human glandular kallikrein, PSA and mitochondria cytochrome C oxidase subunit II cDNAs in pCDNA3.1 were added to the driver DNA and subtraction was performed as described above to provide a second subtracted cDNA library hereinafter referred to as the "subtracted prostate tumor specific cDNA library with spike".

Twenty-two cDNA clones were isolated from the subtracted prostate tumor specific cDNA library with spike. The determined 3' and 5' cDNA sequences for the clones referred to as J1-17, L1-12, N1-1862, J1-13, J1-19, J1-25, J1-24, K1-58, K1-63, L1-4 and L1-14 are provided in SEQ ID NOS: 8-9, 10-11, 12-13, 14-15, 16-17, 18-19, 20-21, 22-23, 24-25, 26-27 and 28-29, respectively. The determined 3' cDNA sequences for the clones referred to as J1-12, J1-16, J1-21, K1-48, K1-55, L1-2, L1-6, N1-1858, N1-1860, N1-1861, N1-1864 are provided in SEQ ID NOS: 30-40, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to three of the five most abundant DNA species, (J1-17, L1-12 and N1-1862; SEQ ID NOS: 8-9, 10-11 and 12-13, respectively). Of the remaining two most abundant species, one (J1-12; SEQ ID NO:30) was found to be identical to the previously identified human pulmonary surfactant-associated protein, and the other (K1-48; SEQ ID NO:33) was determined to have some homology to *R. norvegicus* mRNA for 2-arylpropionyl-CoA epimerase. Of the 17 less abundant cDNA clones isolated from the subtracted prostate tumor specific cDNA library with spike, four (J1-16, K1-55, L1-6 and N1-1864; SEQ ID NOS:31, 34, 36 and 40, respectively) were found to be identical to previously identified sequences, two (J1-21 and N1-1860; SEQ ID NOS: 32 and 38, respectively) were found to show some homology to non-human sequences, and two (L1-2 and N1-1861; SEQ ID NOS: 35 and 39, respectively) were found to show some homology to known human sequences. No significant homologies were found to the polypeptides J1-13, J1-19, J1-24, J1-25, K1-58, K1-63, L1-4, L1-14 (SEQ ID NOS: 14-15, 16-17, 20-21, 18-19, 22-23, 24-25, 26-27, 28-29, respectively).

Subsequent studies led to the isolation of full length cDNA sequences for J1-17, L1-12 and N1-1862 (SEQ ID NOS: 109-111, respectively). The corresponding predicted



amino acid sequences are provided in SEQ ID NOS: 112-114. L1-12 is also referred to as P501S.

In a further experiment, four additional clones were identified by subtracting a prostate tumor cDNA library with normal prostate cDNA prepared from a pool of three normal prostate poly A+ RNA (referred to as "prostate subtraction 2"). The determined cDNA sequences for these clones, hereinafter referred to as U1-3064, U1-3065, V1-3692 and 1A-3905, are provided in SEQ ID NO: 69-72, respectively. Comparison of the determined sequences with those in the gene bank revealed no significant homologies to U1-3065.

A second subtraction with spike (referred to as "prostate subtraction spike 2") was performed by subtracting a prostate tumor specific cDNA library with spike with normal pancreas cDNA library and further spiked with PSA, J1-17, pulmonary surfactant-associated protein, mitochondrial DNA, cytochrome c oxidase subunit II, N1-1862, autonomously replicating sequence, L1-12 and tumor expression enhanced gene. Four additional clones, hereinafter referred to as V1-3686, R1-2330, 1B-3976 and V1-3679, were isolated. The determined cDNA sequences for these clones are provided in SEQ ID NO: 73-76, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to V1-3686 and R1-2330.

Further analysis of the three prostate subtractions described above (prostate subtraction 2, subtracted prostate tumor specific cDNA library with spike, and prostate subtraction spike 2) resulted in the identification of sixteen additional clones, referred to as 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1G-4734, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4810, 1I-4811, 1J-4876, 1K-4884 and 1K-4896. The determined cDNA sequences for these clones are provided in SEQ ID NOS: 77-92, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to 1G-4741, 1G-4734, 1I-4807, 1J-4876 and 1K-4896 (SEQ ID NOS: 79, 81, 87, 90 and 92, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4807, 1J-4876, 1K-4884 and 1K-4896, provided in SEQ ID NOS: 179-188 and 191-193, respectively, and to the determination of additional partial cDNA sequences for 1I-4810 and 1I-4811, provided in SEQ ID NOS: 189 and 190, respectively.

Additional studies with prostate subtraction spike 2 resulted in the isolation of three more clones. Their sequences were determined as described above and compared to the most recent GenBank. All three clones were found to have homology to known genes, which are Cysteine-rich protein, KIAA0242, and KIAA0280 (SEQ ID NO: 317, 319, and 320, respectively). Further analysis of these clones by Synteni microarray (Synteni, Palo Alto, CA) demonstrated that all three clones were over-expressed in most prostate tumors and

prostate BPH, as well as in the majority of normal prostate tissues tested, but low expression in all other normal tissues.

An additional subtraction was performed by subtracting a normal prostate cDNA library with normal pancreas cDNA (referred to as "prostate subtraction 3"). This led to the identification of six additional clones referred to as 1G-4761, 1G-4762, 1H-4766, 1H-4770, 1H-4771 and 1H-4772 (SEQ ID NOS: 93-98). Comparison of these sequences with those in the gene bank revealed no significant homologies to 1G-4761 and 1H-4771 (SEQ ID NOS: 93 and 97, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1G-4761, 1G-4762, 1H-4766 and 1H-4772 provided in SEQ ID NOS: 194-196 and 199, respectively, and to the determination of additional partial cDNA sequences for 1H-4770 and 1H-4771, provided in SEQ ID NOS: 197 and 198, respectively.

Subtraction of a prostate tumor cDNA library, prepared from a pool of polyA+ RNA from three prostate cancer patients, with a normal pancreas cDNA library (prostate subtraction 4) led to the identification of eight clones, referred to as 1D-4297, 1D-4309, 1D-1-4278, 1D-4288, 1D-4283, 1D-4304, 1D-4296 and 1D-4280 (SEQ ID NOS: 99-107). These sequences were compared to those in the gene bank as described above. No significant homologies were found to 1D-4283 and 1D-4304 (SEQ ID NOS: 103 and 104, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1D-4309, 1D-1-4278, 1D-4288, 1D-4283, 1D-4304, 1D-4296 and 1D-4280, provided in SEQ ID NOS: 200-206, respectively.

cDNA clones isolated in prostate subtraction 1 and prostate subtraction 2, described above, were colony PCR amplified and their mRNA expression levels in prostate tumor, normal prostate and in various other normal tissues were determined using microarray technology (Synteni, Palo Alto, CA). Briefly, the PCR amplification products were dotted onto slides in an array format, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, reverse transcribed, and fluorescent-labeled cDNA probes were generated. The microarrays were probed with the labeled cDNA probes, the slides scanned and fluorescence intensity was measured. This intensity correlates with the hybridization intensity. Two clones (referred to as P509S and P510S) were found to be over-expressed in prostate tumor and normal prostate and expressed at low levels in all other normal tissues tested (liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon). The determined cDNA sequences for P509S and P510S are provided in SEQ ID NO: 223 and 224, respectively. Comparison of these sequences with those in the gene bank as described above, revealed some homology to previously identified ESTs.

Additional, studies led to the isolation of the full-length cDNA sequence for P509S. This sequence is provided in SEQ ID NO: 332, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 339.

## EXAMPLE 2

### DETERMINATION OF TISSUE SPECIFICITY OF PROSTATE TUMOR POLYPEPTIDES

Using gene specific primers, mRNA expression levels for the representative prostate tumor polypeptides F1-16, H1-1, J1-17 (also referred to as P502S), L1-12 (also referred to as P501S), F1-12 (also referred to as P504S) and N1-1862 (also referred to as P503S) were examined in a variety of normal and tumor tissues using RT-PCR.

Briefly, total RNA was extracted from a variety of normal and tumor tissues using Trizol reagent as described above. First strand synthesis was carried out using 1-2  $\mu$ g of total RNA with SuperScript II reverse transcriptase (BRL Life Technologies) at 42 °C for one hour. The cDNA was then amplified by PCR with gene-specific primers. To ensure the semi-quantitative nature of the RT-PCR,  $\beta$ -actin was used as an internal control for each of the tissues examined. First, serial dilutions of the first strand cDNAs were prepared and RT-PCR assays were performed using  $\beta$ -actin specific primers. A dilution was then chosen that enabled the linear range amplification of the  $\beta$ -actin template and which was sensitive enough to reflect the differences in the initial copy numbers. Using these conditions, the  $\beta$ -actin levels were determined for each reverse transcription reaction from each tissue. DNA contamination was minimized by DNase treatment and by assuring a negative PCR result when using first strand cDNA that was prepared without adding reverse transcriptase.

mRNA Expression levels were examined in four different types of tumor tissue (prostate tumor from 2 patients, breast tumor from 3 patients, colon tumor, lung tumor), and sixteen different normal tissues, including prostate, colon, kidney, liver, lung, ovary, pancreas, skeletal muscle, skin, stomach, testes, bone marrow and brain. F1-16 was found to be expressed at high levels in prostate tumor tissue, colon tumor and normal prostate, and at lower levels in normal liver, skin and testes, with expression being undetectable in the other tissues examined. H1-1 was found to be expressed at high levels in prostate tumor, lung tumor, breast tumor, normal prostate, normal colon and normal brain, at much lower levels in normal lung, pancreas, skeletal muscle, skin, small intestine, bone marrow, and was not detected in the other tissues tested. J1-17 (P502S) and L1-12 (P501S) appear to be specifically over-expressed in prostate, with both genes being expressed at high levels in prostate tumor and normal prostate but at low to undetectable levels in all the other tissues examined. N1-1862 (P503S) was found to be over-expressed in 60% of prostate tumors and detectable in normal colon and kidney. The RT-PCR results thus indicate that

F1-16, H1-1, J1-17 (P502S), N1-1862 (P503S) and L1-12 (P501S) are either prostate specific or are expressed at significantly elevated levels in prostate.

Further RT-PCR studies showed that F1-12 (P504S) is over-expressed in 60% of prostate tumors, detectable in normal kidney but not detectable in all other tissues tested. Similarly, R1-2330 was shown to be over-expressed in 40% of prostate tumors, detectable in normal kidney and liver, but not detectable in all other tissues tested. U1-3064 was found to be over-expressed in 60% of prostate tumors, and also expressed in breast and colon tumors, but was not detectable in normal tissues.

RT-PCR characterization of R1-2330, U1-3064 and 1D-4279 showed that these three antigens are over-expressed in prostate and/or prostate tumors.

Northern analysis with four prostate tumors, two normal prostate samples, two BPH prostates, and normal colon, kidney, liver, lung, pancreas, skeletal muscle, brain, stomach, testes, small intestine and bone marrow, showed that L1-12 (P501S) is over-expressed in prostate tumors and normal prostate, while being undetectable in other normal tissues tested. J1-17 (P502S) was detected in two prostate tumors and not in the other tissues tested. N1-1862 (P503S) was found to be over-expressed in three prostate tumors and to be expressed in normal prostate, colon and kidney, but not in other tissues tested. F1-12 (P504S) was found to be highly expressed in two prostate tumors and to be undetectable in all other tissues tested.

The microarray technology described above was used to determine the expression levels of representative antigens described herein in prostate tumor, breast tumor and the following normal tissues: prostate, liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon. L1-12 (P501S) was found to be over-expressed in normal prostate and prostate tumor, with some expression being detected in normal skeletal muscle. Both J1-12 and F1-12 (P504S) were found to be over-expressed in prostate tumor, with expression being lower or undetectable in all other tissues tested. N1-1862 (P503S) was found to be expressed at high levels in prostate tumor and normal prostate, and at low levels in normal large intestine and normal colon, with expression being undetectable in all other tissues tested. R1-2330 was found to be over-expressed in prostate tumor and normal prostate, and to be expressed at lower levels in all other tissues tested. 1D-4279 was found to be over-expressed in prostate tumor and normal prostate, expressed at lower levels in normal spinal cord, and to be undetectable in all other tissues tested.

Further microarray analysis to specifically address the extent to which P501S (SEQ ID NO: 110) was expressed in breast tumor revealed moderate over-expression not only in breast tumor, but also in metastatic breast tumor (2/31), with negligible to low expression

in normal tissues. This data suggests that P501S may be over-expressed in various breast tumors as well as in prostate tumors.

The expression levels of 32 ESTs (expressed sequence tags) described by Vasmatazis *et al.* (*Proc. Natl. Acad. Sci. USA* 95:300-304, 1998) in a variety of tumor and normal tissues were examined by microarray technology as described above. Two of these clones (referred to as P1000C and P1001C) were found to be over-expressed in prostate tumor and normal prostate, and expressed at low to undetectable levels in all other tissues tested (normal aorta, thymus, resting and activated PBMC, epithelial cells, spinal cord, adrenal gland, fetal tissues, skin, salivary gland, large intestine, bone marrow, liver, lung, dendritic cells, stomach, lymph nodes, brain, heart, small intestine, skeletal muscle, colon and kidney. The determined cDNA sequences for P1000C and P1001C are provided in SEQ ID NO: 384 and 472, respectively. The sequence of P1001C was found to show some homology to the previously isolated Human mRNA for JM27 protein. No significant homologies were found to the sequence of P1000C.

The expression of the polypeptide encoded by the full length cDNA sequence for F1-12 (also referred to as P504S; SEQ ID NO: 108) was investigated by immunohistochemical analysis. Rabbit-anti-P504S polyclonal antibodies were generated against the full length P504S protein by standard techniques. Subsequent isolation and characterization of the polyclonal antibodies were also performed by techniques well known in the art. Immunohistochemical analysis showed that the P504S polypeptide was expressed in 100% of prostate carcinoma samples tested (n=5).

The rabbit-anti-P504S polyclonal antibody did not appear to label benign prostate cells with the same cytoplasmic granular staining, but rather with light nuclear staining. Analysis of normal tissues revealed that the encoded polypeptide was found to be expressed in some, but not all normal human tissues. Positive cytoplasmic staining with rabbit-anti-P504S polyclonal antibody was found in normal human kidney, liver, brain, colon and lung-associated macrophages, whereas heart and bone marrow were negative.

This data indicates that the P504S polypeptide is present in prostate cancer tissues, and that there are qualitative and quantitative differences in the staining between benign prostatic hyperplasia tissues and prostate cancer tissues, suggesting that this polypeptide may be detected selectively in prostate tumors and therefore be useful in the diagnosis of prostate cancer.

### EXAMPLE 3

#### ISOLATION AND CHARACTERIZATION OF PROSTATE TUMOR POLYPEPTIDES BY PCR-BASED SUBTRACTION

A cDNA subtraction library, containing cDNA from normal prostate subtracted with ten other normal tissue cDNAs (brain, heart, kidney, liver, lung, ovary, placenta, skeletal muscle, spleen and thymus) and then submitted to a first round of PCR amplification, was purchased from Clontech. This library was subjected to a second round of PCR amplification, following the manufacturer's protocol. The resulting cDNA fragments were subcloned into the vector pT7 Blue T-vector (Novagen, Madison, WI) and transformed into XL-1 Blue MRF' *E. coli* (Stratagene). DNA was isolated from independent clones and sequenced using a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A.

Fifty-nine positive clones were sequenced. Comparison of the DNA sequences of these clones with those in the gene bank, as described above, revealed no significant homologies to 25 of these clones, hereinafter referred to as P5, P8, P9, P18, P20, P30, P34, P36, P38, P39, P42, P49, P50, P53, P55, P60, P64, P65, P73, P75, P76, P79 and P84. The determined cDNA sequences for these clones are provided in SEQ ID NO: 41-45, 47-52 and 54-65, respectively. P29, P47, P68, P80 and P82 (SEQ ID NO: 46, 53 and 66-68, respectively) were found to show some degree of homology to previously identified DNA sequences. To the best of the inventors' knowledge, none of these sequences have been previously shown to be present in prostate.

Further studies using the PCR-based methodology described above resulted in the isolation of more than 180 additional clones, of which 23 clones were found to show no significant homologies to known sequences. The determined cDNA sequences for these clones are provided in SEQ ID NO: 115-123, 127, 131, 137, 145, 147-151, 153, 156-158 and 160. Twenty-three clones (SEQ ID NO: 124-126, 128-130, 132-136, 138-144, 146, 152, 154, 155 and 159) were found to show some homology to previously identified ESTs. An additional ten clones (SEQ ID NO: 161-170) were found to have some degree of homology to known genes. Larger cDNA clones containing the P20 sequence represent splice variants of a gene referred to as P703P. The determined DNA sequence for the variants referred to as DE1, DE13 and DE14 are provided in SEQ ID NOS: 171, 175 and 177, respectively, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 172, 176 and 178, respectively. The determined cDNA sequence for an extended spliced form of P703 is provided in SEQ ID NO: 225. The DNA sequences for the splice variants referred to as DE2 and DE6 are provided in SEQ ID NOS: 173 and 174, respectively.

mRNA Expression levels for representative clones in tumor tissues (prostate (n=5), breast (n=2), colon and lung) normal tissues (prostate (n=5), colon, kidney, liver, lung (n=2), ovary (n=2), skeletal muscle, skin, stomach, small intestine and brain), and activated

and non-activated PBMC was determined by RT-PCR as described above. Expression was examined in one sample of each tissue type unless otherwise indicated.

P9 was found to be highly expressed in normal prostate and prostate tumor compared to all normal tissues tested except for normal colon which showed comparable expression. P20, a portion of the P703P gene, was found to be highly expressed in normal prostate and prostate tumor, compared to all twelve normal tissues tested. A modest increase in expression of P20 in breast tumor (n=2), colon tumor and lung tumor was seen compared to all normal tissues except lung (1 of 2). Increased expression of P18 was found in normal prostate, prostate tumor and breast tumor compared to other normal tissues except lung and stomach. A modest increase in expression of P5 was observed in normal prostate compared to most other normal tissues. However, some elevated expression was seen in normal lung and PBMC. Elevated expression of P5 was also observed in prostate tumors (2 of 5), breast tumor and one lung tumor sample. For P30, similar expression levels were seen in normal prostate and prostate tumor, compared to six of twelve other normal tissues tested. Increased expression was seen in breast tumors, one lung tumor sample and one colon tumor sample, and also in normal PBMC. P29 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to the majority of normal tissues. However, substantial expression of P29 was observed in normal colon and normal lung (2 of 2). P80 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to all other normal tissues tested, with increased expression also being seen in colon tumor.

Further studies resulted in the isolation of twelve additional clones, hereinafter referred to as 10-d8, 10-h10, 11-c8, 7-g6, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3, 8-h11, 9-f12 and 9-f3. The determined DNA sequences for 10-d8, 10-h10, 11-c8, 8-d4, 8-d9, 8-h11, 9-f12 and 9-f3 are provided in SEQ ID NO: 207, 208, 209, 216, 217, 220, 221 and 222, respectively. The determined forward and reverse DNA sequences for 7-g6, 8-b5, 8-b6 and 8-g3 are provided in SEQ ID NO: 210 and 211; 212 and 213; 214 and 215; and 218 and 219, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to the sequence of 9-f3. The clones 10-d8, 11-c8 and 8-h11 were found to show some homology to previously isolated ESTs, while 10-h10, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3 and 9-f12 were found to show some homology to previously identified genes. Further characterization of 7-G6 and 8-G3 showed identity to the known genes PAP and PSA, respectively.

mRNA expression levels for these clones were determined using the microarray technology described above. The clones 7-G6, 8-G3, 8-B5, 8-B6, 8-D4, 8-D9, 9-F3, 9-F12, 9-H3, 10-A2, 10-A4, 11-C9 and 11-F2 were found to be over-expressed in prostate tumor and normal prostate, with expression in other tissues tested being low or undetectable.

Increased expression of 8-F11 was seen in prostate tumor and normal prostate, bladder, skeletal muscle and colon. Increased expression of 10-H10 was seen in prostate tumor and normal prostate, bladder, lung, colon, brain and large intestine. Increased expression of 9-B1 was seen in prostate tumor, breast tumor, and normal prostate, salivary gland, large intestine and skin, with increased expression of 11-C8 being seen in prostate tumor, and normal prostate and large intestine.

An additional cDNA fragment derived from the PCR-based normal prostate subtraction, described above, was found to be prostate specific by both micro-array technology and RT-PCR. The determined cDNA sequence of this clone (referred to as 9-A11) is provided in SEQ ID NO: 226. Comparison of this sequence with those in the public databases revealed 99% identity to the known gene HOXB13.

Further studies led to the isolation of the clones 8-C6 and 8-H7. The determined cDNA sequences for these clones are provided in SEQ ID NO: 227 and 228, respectively. These sequences were found to show some homology to previously isolated ESTs.

PCR and hybridization-based methodologies were employed to obtain longer cDNA sequences for clone P20 (also referred to as P703P), yielding three additional cDNA fragments that progressively extend the 5' end of the gene. These fragments, referred to as P703PDE5, P703P6.26, and P703PX-23 (SEQ ID NO: 326, 328 and 330, with the predicted corresponding amino acid sequences being provided in SEQ ID NO: 327, 329 and 331, respectively) contain additional 5' sequence. P703PDE5 was recovered by screening of a cDNA library (#141-26) with a portion of P703P as a probe. P703P6.26 was recovered from a mixture of three prostate tumor cDNAs and P703PX\_23 was recovered from cDNA library (#438-48). Together, the additional sequences include all of the putative mature serine protease along with part of the putative signal sequence. Further studies using a PCR-based subtraction library of a prostate tumor pool subtracted against a pool of normal tissues (referred to as JP: PCR subtraction) resulted in the isolation of thirteen additional clones, seven of which did not share any significant homology to known GenBank sequences. The determined cDNA sequences for these seven clones (P711P, P712P, novel 23, P774P, P775P, P710P and P768P) are provided in SEQ ID NO: 307-311, 313 and 315, respectively. The remaining six clones (SEQ ID NO: 316 and 321-325) were shown to share some homology to known genes. By microarray analysis, all thirteen clones showed three or more fold over-expression in prostate tissues, including prostate tumors, BPH and normal prostate as compared to normal non-prostate tissues. Clones P711P, P712P, novel 23 and P768P showed over-expression in most prostate tumors and BPH tissues tested (n=29), and in the majority of normal prostate tissues (n=4), but background to low expression levels in all normal tissues.



Clones P774P, P775P and P710P showed comparatively lower expression and expression in fewer prostate tumors and BPH samples, with negative to low expression in normal prostate.

The full-length cDNA for P711P was obtained by employing the partial sequence of SEQ ID NO: 307 to screen a prostate cDNA library. Specifically, a directionally cloned prostate cDNA library was prepared using standard techniques. One million colonies of this library were plated onto LB/Amp plates. Nylon membrane filters were used to lift these colonies, and the cDNAs which were picked up by these filters were denatured and cross-linked to the filters by UV light. The P711P cDNA fragment of SEQ ID NO: 307 was radio-labeled and used to hybridize with these filters. Positive clones were selected, and cDNAs were prepared and sequenced using an automatic Perkin Elmer/Applied Biosystems sequencer. The determined full-length sequence of P711P is provided in SEQ ID NO: 382, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 383.

Using PCR and hybridization-based methodologies, additional cDNA sequence information was derived for two clones described above, 11-C9 and 9-F3, herein after referred to as P707P and P714P, respectively (SEQ ID NO: 333 and 334). After comparison with the most recent GenBank, P707P was found to be a splice variant of the known gene HoxB13. In contrast, no significant homologies to P714P were found.

Clones 8-B3, P89, P98, P130 and P201 (as disclosed in U.S. Patent Application No. 09/020,956, filed February 9, 1998) were found to be contained within one contiguous sequence, referred to as P705P (SEQ ID NO: 335, with the predicted amino acid sequence provided in SEQ ID NO: 336), which was determined to be a splice variant of the known gene NKX 3.1.

#### EXAMPLE 4 SYNTHESIS OF POLYPEPTIDES

Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems 430A peptide synthesizer using Fmoc chemistry with HPTU (O-Benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence may be attached to the amino terminus of the peptide to provide a method of conjugation, binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from the solid support may be carried out using the following cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be dissolved in water containing 0.1% trifluoroacetic acid (TFA) and lyophilized prior to purification by C18 reverse phase HPLC. A gradient of 0%-60% acetonitrile (containing 0.1% TFA) in water (containing 0.1% TFA) may be used to elute the peptides. Following

lyophilization of the pure fractions, the peptides may be characterized using electrospray or other types of mass spectrometry and by amino acid analysis.

#### EXAMPLE 5

##### FURTHER ISOLATION AND CHARACTERIZATION OF PROSTATE TUMOR POLYPEPTIDES BY PCR-BASED SUBTRACTION

A cDNA library generated from prostate primary tumor mRNA as described above was subtracted with cDNA from normal prostate. The subtraction was performed using a PCR-based protocol (Clontech), which was modified to generate larger fragments. Within this protocol, tester and driver double stranded cDNA were separately digested with five restriction enzymes that recognize six-nucleotide restriction sites (MluI, MscI, PvuII, SalI and StuI). This digestion resulted in an average cDNA size of 600 bp, rather than the average size of 300 bp that results from digestion with RsaI according to the Clontech protocol. This modification did not affect the subtraction efficiency. Two tester populations were then created with different adapters, and the driver library remained without adapters.

The tester and driver libraries were then hybridized using excess driver cDNA. In the first hybridization step, driver was separately hybridized with each of the two tester cDNA populations. This resulted in populations of (a) unhybridized tester cDNAs, (b) tester cDNAs hybridized to other tester cDNAs, (c) tester cDNAs hybridized to driver cDNAs and (d) unhybridized driver cDNAs. The two separate hybridization reactions were then combined, and rehybridized in the presence of additional denatured driver cDNA. Following this second hybridization, in addition to populations (a) through (d), a fifth population (e) was generated in which tester cDNA with one adapter hybridized to tester cDNA with the second adapter. Accordingly, the second hybridization step resulted in enrichment of differentially expressed sequences which could be used as templates for PCR amplification with adaptor-specific primers.

The ends were then filled in, and PCR amplification was performed using adaptor-specific primers. Only population (e), which contained tester cDNA that did not hybridize to driver cDNA, was amplified exponentially. A second PCR amplification step was then performed, to reduce background and further enrich differentially expressed sequences.

This PCR-based subtraction technique normalizes differentially expressed cDNAs so that rare transcripts that are overexpressed in prostate tumor tissue may be recoverable. Such transcripts would be difficult to recover by traditional subtraction methods.

In addition to genes known to be overexpressed in prostate tumor, seventy-seven further clones were identified. Sequences of these partial cDNAs are provided in SEQ ID NO: 29 to 305. Most of these clones had no significant homology to database sequences. Exceptions were JPTPN23 (SEQ ID NO: 231; similarity to pig valosin-containing protein), JPTPN30 (SEQ ID NO: 234; similarity to rat mRNA for proteasome subunit), JPTPN45 (SEQ ID NO: 243; similarity to rat *norvegicus* cytosolic NADP-dependent isocitrate dehydrogenase), JPTPN46 (SEQ ID NO: 244; similarity to human subclone H8 4 d4 DNA sequence), JP1D6 (SEQ ID NO: 265; similarity to *G. gallus* dynein light chain-A), JP8D6 (SEQ ID NO: 288; similarity to human BAC clone RG016J04), JP8F5 (SEQ ID NO: 289; similarity to human subclone H8 3 b5 DNA sequence), and JP8E9 (SEQ ID NO: 299; similarity to human Alu sequence).

Additional studies using the PCR-based subtraction library consisting of a prostate tumor pool subtracted against a normal prostate pool (referred to as PT-PN PCR subtraction) yielded three additional clones. Comparison of the cDNA sequences of these clones with the most recent release of GenBank revealed no significant homologies to the two clones referred to as P715P and P767P (SEQ ID NO: 312 and 314). The remaining clone was found to show some homology to the known gene KIAA0056 (SEQ ID NO: 318). Using microarray analysis to measure mRNA expression levels in various tissues, all three clones were found to be over-expressed in prostate tumors and BPH tissues. Specifically, clone P715P was over-expressed in most prostate tumors and BPH tissues by a factor of three or greater, with elevated expression seen in the majority of normal prostate samples and in fetal tissue, but negative to low expression in all other normal tissues. Clone P767P was over-expressed in several prostate tumors and BPH tissues, with moderate expression levels in half of the normal prostate samples, and background to low expression in all other normal tissues tested.

Further analysis, by microarray as described above, of the PT-PN PCR subtraction library and of a DNA subtraction library containing cDNA from prostate tumor subtracted with a pool of normal tissue cDNAs, led to the isolation of 27 additional clones (SEQ ID NO: 340-365 and 381) which were determined to be over-expressed in prostate tumor. The clones of SEQ ID NO: 341, 342, 345, 347, 348, 349, 351, 355-359, 361, 362 and 364 were also found to be expressed in normal prostate. Expression of all 26 clones in a variety of normal tissues was found to be low or undetectable, with the exception of P544S (SEQ ID NO: 356) which was found to be expressed in small intestine. Of the 26 clones, 10 (SEQ ID NO: 340-349) were found to show some homology to previously identified sequences. No significant homologies were found to the clones of SEQ ID NO: 350-365.

#### EXAMPLE 6

##### PEPTIDE PRIMING OF MICE AND PROPAGATION OF CTL LINES

6.1. This Example illustrates the preparation of a CTL cell line specific for cells expressing the P502S gene.

Mice expressing the transgene for human HLA A2.1 (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with P2S#12 peptide (VLGWVAEL; SEQ ID NO: 306), which is derived from the P502S gene (also referred to herein as J1-17, SEQ ID NO: 8), as described by Theobald et al., *Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995 with the following modifications. Mice were immunized with 100µg of P2S#12 and 120µg of an I-A<sup>b</sup> binding peptide derived from hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and using a nylon mesh single cell suspensions prepared. Cells were then resuspended at  $6 \times 10^6$  cells/ml in complete media (RPMI-1640; Gibco BRL, Gaithersburg, MD) containing 10% FCS, 2mM Glutamine (Gibco BRL), sodium pyruvate (Gibco BRL), non-essential amino acids (Gibco BRL),  $2 \times 10^{-5}$  M 2-mercaptoethanol, 50U/ml penicillin and streptomycin, and cultured in the presence of irradiated (3000 rads) P2S#12-pulsed (5mg/ml P2S#12 and 10mg/ml  $\beta$ 2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7µg/ml dextran sulfate and 25µg/ml LPS for 3 days). Six days later, cells ( $5 \times 10^5$ /ml) were restimulated with  $2.5 \times 10^6$ /ml peptide pulsed irradiated (20,000 rads) EL4A2Kb cells (Sherman et al, *Science* 258:815-818, 1992) and  $3 \times 10^6$ /ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20U/ml IL-2. Cells continued to be restimulated on a weekly basis as described, in preparation for cloning the line.

P2S#12 line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb tumor cells ( $1 \times 10^4$  cells/ well) as stimulators and A2 transgenic spleen cells as feeders ( $5 \times 10^5$  cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were

restimulated as before. On day 21, clones that were growing were isolated and maintained in culture. Several of these clones demonstrated significantly higher reactivity (lysis) against human fibroblasts (HLA A2.1 expressing) transduced with P502S than against control fibroblasts. An example is presented in Figure 1.

This data indicates that P2S #12 represents a naturally processed epitope of the P502S protein that is expressed in the context of the human HLA A2.1 molecule.

6.2. This Example illustrates the preparation of murine CTL lines and CTL clones specific for cells expressing the P501S gene.

This series of experiments were performed similarly to that described above. Mice were immunized with the P1S#10 peptide (SEQ ID NO: 337), which is derived from the P501S gene (also referred to herein as L1-12, SEQ ID NO: 110). The P1S#10 peptide was derived by analysis of the predicted polypeptide sequence for P501S for potential HLA-A2 binding sequences as defined by published HLA-A2 binding motifs (Parker, KC, *et al*, *J. Immunol.*, 152:163, 1994). P1S#10 peptide was synthesized as described in Example 4, and empirically tested for HLA-A2 binding using a T cell based competition assay. Predicted A2 binding peptides were tested for their ability to compete HLA-A2 specific peptide presentation to an HLA-A2 restricted CTL clone (D150M58), which is specific for the HLA-A2 binding influenza matrix peptide fluM58. D150M58 CTL secretes TNF in response to self-presentation of peptide fluM58. In the competition assay, test peptides at 100-200  $\mu\text{g/ml}$  were added to cultures of D150M58 CTL in order to bind HLA-A2 on the CTL. After thirty minutes, CTL cultured with test peptides, or control peptides, were tested for their antigen dose response to the fluM58 peptide in a standard TNF bioassay. As shown in Figure 3, peptide P1S#10 competes HLA-A2 restricted presentation of fluM58, demonstrating that peptide P1S#10 binds HLA-A2.

Mice expressing the transgene for human HLA A2.1 were immunized as described by Theobald *et al.* (*Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995) with the following modifications. Mice were immunized with 62.5 $\mu\text{g}$  of P1S #10 and 120 $\mu\text{g}$  of an I-A<sup>b</sup> binding peptide derived from Hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and single cell suspensions prepared using a nylon mesh. Cells were then resuspended at  $6 \times 10^6$  cells/ml in complete media (as described above) and cultured in the presence of irradiated (3000 rads) P1S#10-pulsed (2 $\mu\text{g/ml}$  P1S#10 and 10mg/ml  $\beta$ 2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7 $\mu\text{g/ml}$  dextran sulfate and 25 $\mu\text{g/ml}$  LPS for 3 days). Six days later cells ( $5 \times 10^5/\text{ml}$ ) were restimulated with  $2.5 \times 10^6/\text{ml}$  peptide-pulsed irradiated (20,000 rads) EL4A2Kb cells, as described above, and  $3 \times 10^6/\text{ml}$  A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20 U/ml IL-2. Cells were restimulated on a weekly

basis in preparation for cloning. After three rounds of *in vitro* stimulations, one line was generated that recognized P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat targets as shown in Figure 4.

A P1S#10-specific CTL line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb tumor cells ( $1 \times 10^4$  cells/ well) as stimulators and A2 transgenic spleen cells as feeders ( $5 \times 10^5$  cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, viable clones were isolated and maintained in culture. As shown in Figure 5, five of these clones demonstrated specific cytolytic reactivity against P501S-transduced Jurkat A2Kb targets. This data indicates that P1S#10 represents a naturally processed epitope of the P501S protein that is expressed in the context of the human HLA-A2.1 molecule.

#### EXAMPLE 7

##### ABILITY OF HUMAN T CELLS TO RECOGNIZE PROSTATE TUMOR POLYPEPTIDES

This Example illustrates the ability of T cells specific for a prostate tumor polypeptide to recognize human tumor.

Human CD8<sup>+</sup> T cells were primed *in vitro* to the P2S-12 peptide (SEQ ID NO: 306) derived from P502S (also referred to as J1-17) using dendritic cells according to the protocol of Van Tsai et al. (*Critical Reviews in Immunology* 18:65-75, 1998). The resulting CD8<sup>+</sup> T cell microcultures were tested for their ability to recognize the P2S-12 peptide presented by autologous fibroblasts or fibroblasts which were transduced to express the P502S gene in a  $\gamma$ -interferon ELISPOT assay (*see* Lalvani et al., *J. Exp. Med.* 186:859-865, 1997). Briefly, titrating numbers of T cells were assayed in duplicate on  $10^4$  fibroblasts in the presence of 3  $\mu$ g/ml human  $\beta_2$ -microglobulin and 1  $\mu$ g/ml P2S-12 peptide or control E75 peptide. In addition, T cells were simultaneously assayed on autologous fibroblasts transduced with the P502S gene or as a control, fibroblasts transduced with HER-2/*neu*. Prior to the assay, the fibroblasts were treated with 10 ng/ml  $\gamma$ -interferon for 48 hours to upregulate class I MHC expression. One of the microcultures (#5) demonstrated strong recognition of both peptide pulsed fibroblasts as well as transduced fibroblasts in a  $\gamma$ -interferon ELISPOT assay. Figure 2A demonstrates that there was a strong increase in the number of  $\gamma$ -interferon spots with increasing numbers of T cells on fibroblasts pulsed with the P2S-12 peptide (solid bars) but not with the control E75 peptide (open bars). This shows the ability of these T cells to specifically recognize the P2S-12 peptide. As shown in Figure 2B, this microculture also demonstrated an increase in the number of  $\gamma$ -interferon spots with increasing numbers of T

cells on fibroblasts transduced to express the P502S gene but not the HER-2/*neu* gene. These results provide additional confirmatory evidence that the P2S-12 peptide is a naturally processed epitope of the P502S protein. Furthermore, this also demonstrates that there exists in the human T cell repertoire, high affinity T cells which are capable of recognizing this epitope. These T cells should also be capable of recognizing human tumors which express the P502S gene.

#### EXAMPLE 8

##### PRIMING OF CTL *IN VIVO* USING NAKED DNA IMMUNIZATION WITH A PROSTATE ANTIGEN

The prostate tumor antigen L1-12, as described above, is also referred to as P501S. HLA A2Kb Tg mice (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with 100 µg VR10132-P501S either intramuscularly or intradermally. The mice were immunized three times, with a two week interval between immunizations. Two weeks after the last immunization, immune spleen cells were cultured with Jurkat A2Kb-P501S transduced stimulator cells. CTL lines were stimulated weekly. After two weeks of *in vitro* stimulation, CTL activity was assessed against P501S transduced targets. Two out of 8 mice developed strong anti-P501S CTL responses. These results demonstrate that P501S contains at least one naturally processed A2-restricted CTL epitope.

#### EXAMPLE 9

##### GENERATION OF HUMAN CTL *IN VITRO* USING WHOLE GENE PRIMING AND STIMULATION TECHNIQUES WITH PROSTATE TUMOR ANTIGEN

Using *in vitro* whole-gene priming with P501S-retrovirally transduced autologous fibroblasts (see, for example, Yee et al, *The Journal of Immunology*, 157(9):4079-86, 1996), human CTL lines were derived that specifically recognize autologous fibroblasts transduced with P501S (also known as L1-12), as determined by interferon-γ ELISPOT analysis as described above. Using a panel of HLA-mismatched fibroblast lines transduced with P501S, these CTL lines were shown to be restricted HLA-A2 class I allele. Specifically, dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal human donors by growing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, DC were infected overnight with recombinant P501S vaccinia virus at a multiplicity of infection (M.O.I) of five, and matured overnight by the addition of 3 µg/ml CD40 ligand. Virus was inactivated by UV irradiation. CD8+ T cells were isolated using a magnetic bead system, and

priming cultures were initiated using standard culture techniques. Cultures were restimulated every 7-10 days using autologous primary fibroblasts retrovirally transduced with P501S. Following four stimulation cycles, CD8+ T cell lines were identified that specifically produced interferon- $\gamma$  when stimulated with P501S-transduced autologous fibroblasts. The P501S-specific activity could be sustained by the continued stimulation of the cultures with P501S-transduced fibroblasts in the presence of IL-15. A panel of HLA-mismatched fibroblast lines transduced with P501S were generated to define the restriction allele of the response. By measuring interferon- $\gamma$  in an ELISPOT assay, the P501S specific response was shown to be restricted by HLA-A2. These results demonstrate that a CD8+ CTL response to P501S can be elicited.

#### EXAMPLE 10

##### IDENTIFICATION OF A NATURALLY PROCESSED CTL EPITOPE CONTAINED WITHIN A PROSTATE TUMOR ANTIGEN

The 9-mer peptide p5 (SEQ ID NO: 338) was derived from the P703P antigen (also referred to as P20). The p5 peptide is immunogenic in human HLA-A2 donors and is a naturally processed epitope. Antigen specific CD8+ T cells can be primed following repeated *in vitro* stimulations with monocytes pulsed with p5 peptide. These CTL specifically recognize p5-pulsed target cells in both ELISPOT (as described above) and chromium release assays. Additionally, immunization of HLA-A2 transgenic mice with p5 leads to the generation of CTL lines which recognize a variety of P703P transduced target cells expressing either HLA-A2Kb or HLA-A2. Specifically, HLA-A2 transgenic mice were immunized subcutaneously in the footpad with 100  $\mu$ g of p5 peptide together with 140  $\mu$ g of hepatitis B virus core peptide (a Th peptide) in Freund's incomplete adjuvant. Three weeks post immunization, spleen cells from immunized mice were stimulated *in vitro* with peptide-pulsed LPS blasts. CTL activity was assessed by chromium release assay five days after primary *in vitro* stimulation. Retrovirally transduced cells expressing the control antigen P703P and HLA-A2Kb were used as targets. CTL lines that specifically recognized both p5-pulsed targets as well as P703P-expressing targets were identified.

Human *in vitro* priming experiments demonstrated that the p5 peptide is immunogenic in humans. Dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal human donors by culturing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, the DC were pulsed with p5 peptide and cultured with GM-CSF and IL-4 together with CD8+ T cell enriched PBMC. CTL lines were restimulated on a weekly basis



with p5-pulsed monocytes. Five to six weeks after initiation of the CTL cultures, CTL recognition of p5-pulsed target cells was demonstrated.

#### EXAMPLE 11

##### EXPRESSION OF A BREAST TUMOR-DERIVED ANTIGEN IN PROSTATE

Isolation of the antigen B305D from breast tumor by differential display is described in US Patent Application No. 08/700,014, filed August 20, 1996. Several different splice forms of this antigen were isolated. The determined cDNA sequences for these splice forms are provided in SEQ ID NO: 366-375, with the predicted amino acid sequences corresponding to the sequences of SEQ ID NO: 292, 298 and 301-303 being provided in SEQ ID NO: 299-306, respectively.

The expression levels of B305D in a variety of tumor and normal tissues were examined by real time PCR and by Northern analysis. The results indicated that B305D is highly expressed in breast tumor, prostate tumor, normal prostate tumor and normal testes, with expression being low or undetectable in all other tissues examined (colon tumor, lung tumor, ovary tumor, and normal bone marrow, colon, kidney, liver, lung, ovary, skin, small intestine, stomach).

#### EXAMPLE 12

##### ELICITATION OF PROSTATE TUMOR ANTIGEN-SPECIFIC CTL RESPONSES IN HUMAN BLOOD

This Example illustrates the ability of a prostate tumor antigen to elicit a CTL response in blood of normal humans.

Autologous dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal donors by growth for five days in RPMI medium containing 10% human serum, 50 ng/ml GM-CSF and 30 ng/ml IL-4. Following culture, DC were infected overnight with recombinant P501S-expressing vaccinia virus at an M.O.I. of 5 and matured for 8 hours by the addition of 2 micrograms/ml CD40 ligand. Virus was inactivated by UV irradiation, CD8<sup>+</sup> cells were isolated by positive selection using magnetic beads, and priming cultures were initiated in 24-well plates. Following five stimulation cycles, CD8<sup>+</sup> lines were identified that specifically produced interferon-gamma when stimulated with autologous P501S-transduced fibroblasts. The P501S-specific activity of cell line 3A-1 could be maintained following additional stimulation cycles on autologous B-LCL transduced with P501S. Line 3A-1 was shown to specifically recognize autologous B-LCL transduced to

express P501S, but not EGFP-transduced autologous B-LCL, as measured by cytotoxicity assays ( $^{51}\text{Cr}$  release) and interferon-gamma production (Interferon-gamma Elispot; *see above* and Lalvani et al., *J. Exp. Med.* 186:859-865, 1997). The results of these assays are presented in Figures 6A and 6B.

### EXAMPLE 13

#### IDENTIFICATION OF PROSTATE TUMOR ANTIGENS BY MICROARRAY ANALYSIS

This Example describes the isolation of certain prostate tumor polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened using microarray analysis to identify clones that display at least a three fold over-expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 372 clones were identified, and 319 were successfully sequenced. Table I presents a summary of these clones, which are shown in SEQ ID NOs:385-400. Of these sequences SEQ ID NOs:386, 389, 390 and 392 correspond to novel genes, and SEQ ID NOs: 393 and 396 correspond to previously identified sequences. The others (SEQ ID NOs:385, 387, 388, 391, 394, 395 and 397-400) correspond to known sequences, as shown in Table I.

Table I  
Summary of Prostate Tumor Antigens

Known Genes	Previously identified Genes	Novel Genes
T-cell gamma chain	P504S	23379 (SEQ ID NO:389)
Kallikrein	P1000C	23399 (SEQ ID NO:392)
Vector	P501S	23320 (SEQ ID NO:386)
CGI-82 protein mRNA (23319; SEQ ID NO:385)	P503S	23381 (SEQ ID NO:390)
PSA	P510S	
Ald. 6 Dehyd.	P784P	
L-iditol-2 dehydrogenase (23376; SEQ ID NO:388)	P502S	
Ets transcription factor PDEF (22672; SEQ ID NO:398)	P706P	
hTGR (22678; SEQ ID NO:399)	19142.2, bangur.seq (22621; SEQ ID NO:396)	
KIAA0295(22685; SEQ ID NO:400)	5566.1 Wang(23404; SEQ ID NO:393)	
Prostatic Acid Phosphatase(22655; SEQ ID NO:397)	P712P	

transglutaminase (22611; SEQ ID NO:395)	P778P	
HDLBP (23508; SEQ ID NO:394)		
CGI-69 Protein(23367; SEQ ID NO:387)		
KIAA0122(23383; SEQ ID NO:391)		
TEEG		

CGI-82 showed 4.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 43% of prostate tumors, 25% normal prostate, not detected in other normal tissues tested. L-iditol-2 dehydrogenase showed 4.94 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 90% of prostate tumors, 100% of normal prostate, and not detected in other normal tissues tested. Ets transcription factor PDEF showed 5.55 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% prostate tumors, 25% normal prostate and not detected in other normal tissues tested. hTGR1 showed 9.11 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 63% of prostate tumors and is not detected in normal tissues tested including normal prostate. KIAA0295 showed 5.59 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% of prostate tumors, low to undetectable in normal tissues tested including normal prostate tissues. Prostatic acid phosphatase showed 9.14 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 67% of prostate tumors, 50% of normal prostate, and not detected in other normal tissues tested. Transglutaminase showed 14.84 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 30% of prostate tumors, 50% of normal prostate, and is not detected in other normal tissues tested. High density lipoprotein binding protein (HDLBP) showed 28.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% of normal prostate, and is undetectable in all other normal tissues tested. CGI-69 showed 3.56 fold over-expression in prostate tissues as compared to other normal tissues tested. It is a low abundant gene, detected in more than 90% of prostate tumors, and in 75% normal prostate tissues. The expression of this gene in normal tissues was very low. KIAA0122 showed 4.24 fold over-expression in prostate

tissues as compared to other normal tissues tested. It was over-expressed in 57% of prostate tumors, it was undetectable in all normal tissues tested including normal prostate tissues. 19142.2 bangur showed 23.25 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors and 100% of normal prostate. It was undetectable in other normal tissues tested. 5566.1 Wang showed 3.31 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% normal prostate and was also over-expressed in normal bone marrow, pancreas, and activated PBMC. Novel clone 23379 showed 4.86 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in 97% of prostate tumors and 75% normal prostate and is undetectable in all other normal tissues tested. Novel clone 23399 showed 4.09 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 27% of prostate tumors and was undetectable in all normal tissues tested including normal prostate tissues. Novel clone 23320 showed 3.15 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in all prostate tumors and 50% of normal prostate tissues. It was also expressed in normal colon and trachea. Other normal tissues do not express this gene at high level.

#### EXAMPLE 14

##### IDENTIFICATION OF PROSTATE TUMOR ANTIGENS BY ELECTRONIC SUBTRACTION

This Example describes the use of an electronic subtraction technique to identify prostate tumor antigens.

Potential prostate-specific genes present in the GenBank human EST database were identified by electronic subtraction (similar to that described by Vasmatzis et al., *Proc. Natl. Acad. Sci. USA* 95:300-304, 1998). The sequences of EST clones (43,482) derived from various prostate libraries were obtained from the GenBank public human EST database. Each prostate EST sequence was used as a query sequence in a BLASTN (National Center for Biotechnology Information) search against the human EST database. All matches considered identical (length of matching sequence >100 base pairs, density of identical matches over this region > 70%) were grouped (aligned) together in a cluster. Clusters containing more than 200 ESTs were discarded since they probably represented repetitive elements or highly expressed genes such as those for ribosomal proteins. If two or more clusters shared common ESTs, those clusters were grouped together into a "supercluster," resulting in 4,345 prostate superclusters.

Records for the 479 human cDNA libraries represented in the GenBank release were downloaded to create a database of these cDNA library records. These 479 cDNA libraries were grouped into three groups, Plus (normal prostate and prostate tumor libraries, and breast cell lines, in which expression was desired), Minus (libraries from other normal adult tissues, in which expression was not desirable), and Other (fetal tissue, infant tissue, tissues found only in women, non-prostate tumors and cell lines other than prostate cell lines, in which expression was considered to be irrelevant). A summary of these library groups is presented in Table II.

Table II  
Prostate cDNA Libraries and ESTs

Library	# of Libraries	# of ESTs
Plus	25	43,482
Normal	11	18,875
Tumor	11	21,769
Cell lines	3	2,838
Minus	166	
Other	287	

Each supercluster was analyzed in terms of the ESTs within the supercluster. The tissue source of each EST clone was noted and used to classify the superclusters into four groups: Type 1- EST clones found in the Plus group libraries only; no expression detected in Minus or Other group libraries; Type 2- EST clones found in the Plus and Other group libraries only; no expression detected in the Minus group; Type 3- EST clones found in the Plus, Minus and Other group libraries, but the expression in the Plus group is higher than in either the Minus or Other groups; and Type 4- EST clones found in Plus, Minus and Other group libraries, but the expression in the Plus group is higher than the expression in the Minus group. This analysis identified 4,345 breast clusters (*see* Table III). From these clusters, 3,172 EST clones were ordered from Research Genetics, Inc., and were received as frozen glycerol stocks in 96-well plates.

**Table III**  
**Prostate Cluster Summary**

Type	# of Superclusters	# of ESTs Ordered
1	688	677
2	2899	2484
3	85	11
4	673	0
Total	4345	3172

The inserts were PCR-amplified using amino-linked PCR primers for Synteni microarray analysis. When more than one PCR product was obtained for a particular clone, that PCR product was not used for expression analysis. In total, 2,528 clones from the electronic subtraction method were analyzed by microarray analysis to identify electronic subtraction breast clones that had high tumor vs. normal tissue mRNA. Such screens were performed using a Synteni (Palo Alto, CA) microarray, according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Within these analyses, the clones were arrayed on the chip, which was then probed with fluorescent probes generated from normal and tumor prostate cDNA, as well as various other normal tissues. The slides were scanned and the fluorescence intensity was measured.

Clones with an expression ratio greater than 3 (*i.e.*, the level in prostate tumor cDNA was at least three times the level in normal prostate cDNA) were identified as prostate tumor-specific sequences (Table IV). The sequences of these clones are provided in SEQ ID NOs:401-453, with certain novel sequences shown in SEQ ID NOs:407, 413, 416-419, 422, 426, 427 and 450.

**Table IV**  
**Prostate-tumor Specific Clones**

SEQ ID NO.	Sequence Designation	Comments
401	22545	previously identified P1000C
402	22547	previously identified P704P

403	22548	known
404	22550	known
405	22551	PSA
406	22552	prostate secretory protein 94
407	22553	novel
408	22558	previously identified P509S
409	22562	glandular kallikrein
410	22565	previously identified P1000C
411	22567	PAP
412	22568	B1006C (breast tumor antigen)
413	22570	novel
414	22571	PSA
415	22572	previously identified P706P
416	22573	novel
417	22574	novel
418	22575	novel
419	22580	novel
420	22581	PAP
421	22582	prostatic secretory protein 94
422	22583	novel
423	22584	prostatic secretory protein 94
424	22585	prostatic secretory protein 94
425	22586	known
426	22587	novel
427	22588	novel
428	22589	PAP
429	22590	known
430	22591	PSA
431	22592	known
432	22593	Previously identified P777P
433	22594	T cell receptor gamma chain
434	22595	Previously identified P705P
435	22596	Previously identified P707P
436	22847	PAP
437	22848	known
438	22849	prostatic secretory protein 57



439	22851	PAP
440	22852	PAP
441	22853	PAP
442	22854	previously identified P509S
443	22855	previously identified P705P
444	22856	previously identified P774P
445	22857	PSA
446	23601	previously identified P777P
447	23602	PSA
448	23605	PSA
449	23606	PSA
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451	23614	PSA
452	23618	previously identified P1000C
453	23622	previously identified P705P

#### EXAMPLE 15

##### FURTHER IDENTIFICATION OF PROSTATE TUMOR ANTIGENS BY MICROARRAY ANALYSIS

This Example describes the isolation of additional prostate tumor polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened using microarray analysis to identify clones that display at least a three fold over-expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 142 clones were identified and sequenced. Certain of these clones are shown in SEQ ID NOs:454-467. Of these sequences SEQ ID NOs:459-461 correspond to novel genes. The others (SEQ ID NOs:454-458 and 461-467) correspond to known sequences.

#### EXAMPLE 16

##### FURTHER CHARACTERIZATION OF PROSTATE TUMOR ANTIGEN P710P

This Example describes the full length cloning of P710P.

The prostate cDNA library described above was screened with the P710P fragment described above. One million colonies were plated on LB/Ampicillin plates. Nylon membrane filters were used to lift these colonies, and the cDNAs picked up by these filters were then denatured and cross-linked to the filters by UV light. The P710P fragment was radiolabeled and used to hybridize with the filters. Positive cDNA clones were selected and their cDNAs recovered and sequenced by an automatic ABI Sequencer. Four sequences were obtained, and are presented in SEQ ID NOs:468-471.

From the foregoing, it will be appreciated that, although specific embodiments of the invention have been described herein for the purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the present invention is not limited except as by the appended claims.

## CLAIMS

1. An isolated polypeptide comprising at least an immunogenic portion of a prostate tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(a) sequences recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472;

(b) sequences that hybridize to any of the foregoing sequences under moderately stringent conditions; and

(c) complements of any of the sequence of (a) or (b).

2. An isolated polypeptide according to claim 1, wherein the polypeptide comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472, or a complement of any of the foregoing polynucleotide sequences.

3. An isolated polypeptide comprising a sequence recited in any one of SEQ ID NO: 108, 112, 113, 114, 172, 176, 178, 327, 329, 331, 339 and 383.

4. An isolated polynucleotide encoding at least 15 amino acid residues of a prostate tumor protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434,

435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472, or a complement of any of the foregoing sequences.

5. An isolated polynucleotide encoding a prostate tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472, or a complement of any of the foregoing sequences.

6. An isolated polynucleotide comprising a sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472.

7. An isolated polynucleotide comprising a sequence that hybridizes, under moderately stringent conditions, to a sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472.

8. An isolated polynucleotide complementary to a polynucleotide according to any one of claims 4-7.

9. An expression vector comprising a polynucleotide according to any one of claims 4-7.

10. A host cell transformed or transfected with an expression vector according to claim 9.

11. An expression vector comprising a polynucleotide according claim 8.

12. A host cell transformed or transfected with an expression vector according to claim 11.

13. A pharmaceutical composition comprising a polypeptide according to claim 1, in combination with a physiologically acceptable carrier.

14. A vaccine comprising a polypeptide according to claim 1, in combination with a non-specific immune response enhancer.

15. A vaccine according to claim 14, wherein the non-specific immune response enhancer is an adjuvant.

16. A vaccine according to claim 14, wherein the non-specific immune response enhancer induces a predominantly Type I response.

17. A pharmaceutical composition comprising a polynucleotide according to claim 4, in combination with a physiologically acceptable carrier.

18. A vaccine comprising a polynucleotide according to claim 4, in combination with a non-specific immune response enhancer.

19. A vaccine according to claim 18, wherein the non-specific immune response enhancer is an adjuvant.

20. A vaccine according to claim 18, wherein the non-specific immune response enhancer induces a predominantly Type I response.

21. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a prostate tumor protein that comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472 or a complement of any of the foregoing polynucleotide sequences.

22. A pharmaceutical composition comprising an antibody or fragment thereof according to claim 18, in combination with a physiologically acceptable carrier.

23. A pharmaceutical composition comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with a pharmaceutically acceptable carrier or excipient.

24. A pharmaceutical composition according to claim 23, wherein the antigen presenting cell is a dendritic cell or a macrophage.

25. A vaccine comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with a non-specific immune response enhancer.

26. A vaccine according to claim 25, wherein the non-specific immune response enhancer is an adjuvant.

27. A vaccine according to claim 25, wherein the non-specific immune response enhancer induces a predominantly Type I response.

28. A vaccine according to claim 25, wherein the antigen-presenting cell is a dendritic cell.

29. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a polypeptide according to claim 1, and thereby inhibiting the development of a cancer in the patient.

30. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a polynucleotide according to claim 4, and thereby inhibiting the development of a cancer in the patient.

31. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of an antibody or antigen-binding fragment thereof according to claim 21, and thereby inhibiting the development of a cancer in the patient.

32. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of an antigen-presenting cell that expresses a polypeptide according to claim 1, and thereby inhibiting the development of a cancer in the patient.

33. A method according to claim 32, wherein the antigen-presenting cell is a dendritic cell.

34. A method according to any one of claims 29-32, wherein the cancer is prostate cancer.

35. A fusion protein comprising at least one polypeptide according to claim 1.

36. A fusion protein according to claim 35, wherein the fusion protein comprises an expression enhancer that increases expression of the fusion protein in a host cell transfected with a polynucleotide encoding the fusion protein.

37. A fusion protein according to claim 35, wherein the fusion protein comprises a T helper epitope that is not present within the polypeptide of claim 1.

38. A fusion protein according to claim 35, wherein the fusion protein comprises an affinity tag.

39. An isolated polynucleotide encoding a fusion protein according to claim 35.

40. A pharmaceutical composition comprising a fusion protein according to claim 32, in combination with a physiologically acceptable carrier.

41. A vaccine comprising a fusion protein according to claim 35, in combination with a non-specific immune response enhancer.

42. A vaccine according to claim 41, wherein the non-specific immune response enhancer is an adjuvant.

43. A vaccine according to claim 41, wherein the non-specific immune response enhancer induces a predominantly Type I response.

44. A pharmaceutical composition comprising a polynucleotide according to claim 40, in combination with a physiologically acceptable carrier.

45. A vaccine comprising a polynucleotide according to claim 40, in combination with a non-specific immune response enhancer.

46. A vaccine according to claim 45, wherein the non-specific immune response enhancer is an adjuvant.

47. A vaccine according to claim 45, wherein the non-specific immune response enhancer induces a predominantly Type I response.

48. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a pharmaceutical composition according to claim 40 or claim 44.

49. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a vaccine according to claim 41 or claim 45.

50. A method for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a prostate tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(i) polynucleotides recited in any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472; and

(ii) complements of the foregoing polynucleotides;

wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the prostate tumor protein from the sample.

51. A method according to claim 50, wherein the biological sample is blood or a fraction thereof.



52. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated according to the method of claim 50.

53. A method for stimulating and/or expanding T cells specific for a prostate tumor protein, comprising contacting T cells with one or more of:

- (i) a polypeptide according to claim 1;
  - (ii) a polypeptide encoded by a polynucleotide comprising a sequence provided in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472;
  - (iii) a polynucleotide encoding a polypeptide of (i) or (ii); and/or
  - (iv) an antigen presenting cell that expresses a polypeptide of (i) or (ii);
- under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.

54. An isolated T cell population, comprising T cells prepared according to the method of claim 53.

55. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population according to claim 54.

56. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

- (a) incubating CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient with at least one component selected from the group consisting of:
  - (i) a polypeptide according to claim 1;
  - (ii) a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472;
  - (iii) a polynucleotide encoding a polypeptide of (i) or (ii); or
  - (iv) an antigen-presenting cell that expresses a polypeptide of (i) or (ii);

such that T cells proliferate; and

- (b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient.

57. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient with at least one component selected from the group consisting of:

- (i) a polypeptide according to claim 1;
- (ii) a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472;
- (iii) a polynucleotide encoding a polypeptide of (i) or (ii); or
- (iv) an antigen-presenting cell that expresses a polypeptide of (i) or (ii);

such that T cells proliferate;

- (b) cloning at least one proliferated cell; and
- (c) administering to the patient an effective amount of the cloned T cells, and thereby inhibiting the development of a cancer in the patient.

58. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient with a binding agent that binds to a prostate tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(i) polynucleotides recited in any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472; and

(ii) complements of the foregoing polynucleotides;

- (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and
- (c) comparing the amount of polypeptide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

59. A method according to claim 58, wherein the binding agent is an antibody.

60. A method according to claim 59, wherein the antibody is a monoclonal antibody.

61. A method according to claim 58, wherein the cancer is prostate cancer.
62. A method for monitoring the progression of a cancer in a patient, comprising the steps of:
- (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a prostate tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472, or a complement of any of the foregoing polynucleotides;
  - (b) detecting in the sample an amount of polypeptide that binds to the binding agent;
  - (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and
  - (d) comparing the amount of polypeptide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.
63. A method according to claim 62, wherein the binding agent is an antibody.
64. A method according to claim 63, wherein the antibody is a monoclonal antibody.
65. A method according to claim 62, wherein the cancer is a prostate cancer.
66. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:
- (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472, or a complement of any of the foregoing polynucleotides;
  - (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and

(c) comparing the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

67. A method according to claim 66, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

68. A method according to claim 66, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

69. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472, or a complement of any of the foregoing polynucleotides;

(b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide;

(c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and

(d) comparing the amount of polynucleotide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

70. A method according to claim 69, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

71. A method according to claim 69, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

72. A diagnostic kit, comprising:

(a) one or more antibodies according to claim 21; and

(b) a detection reagent comprising a reporter group.

73. A kit according to claim 72, wherein the antibodies are immobilized on a solid support.

74. A kit according to claim 73, wherein the solid support comprises nitrocellulose, latex or a plastic material.

75. A kit according to claim 72, wherein the detection reagent comprises an anti-immunoglobulin, protein G, protein A or lectin.

76. A kit according to claim 72, wherein the reporter group is selected from the group consisting of radioisotopes, fluorescent groups, luminescent groups, enzymes, biotin and dye particles.

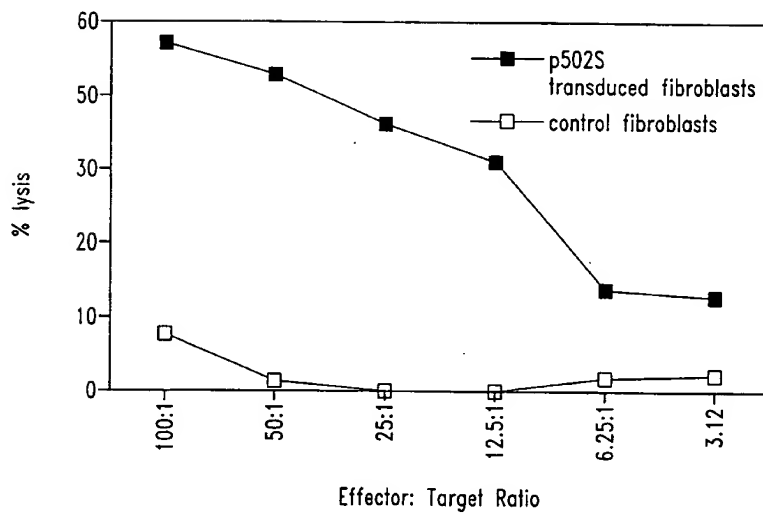
77. An oligonucleotide comprising 10 to 40 nucleotides that hybridize under moderately stringent conditions to a polynucleotide that encodes a prostate tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472, or a complement of any of the foregoing polynucleotides.

78. A oligonucleotide according to claim 77, wherein the oligonucleotide comprises 10-40 nucleotides recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472.

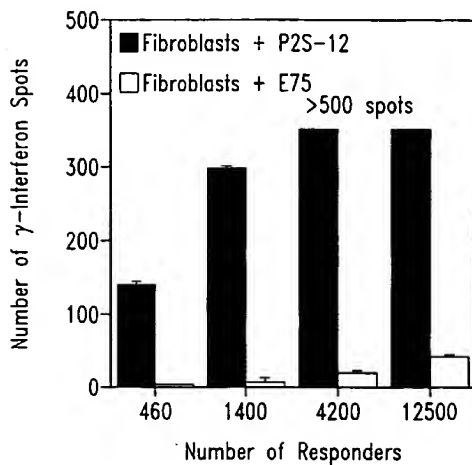
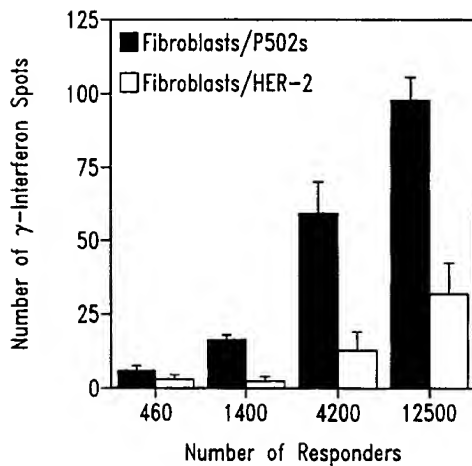
79. A diagnostic kit, comprising:

- (a) an oligonucleotide according to claim 77; and
- (b) a diagnostic reagent for use in a polymerase chain reaction or hybridization assay.

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*Fig. 1*

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*Fig. 2A**Fig. 2B*

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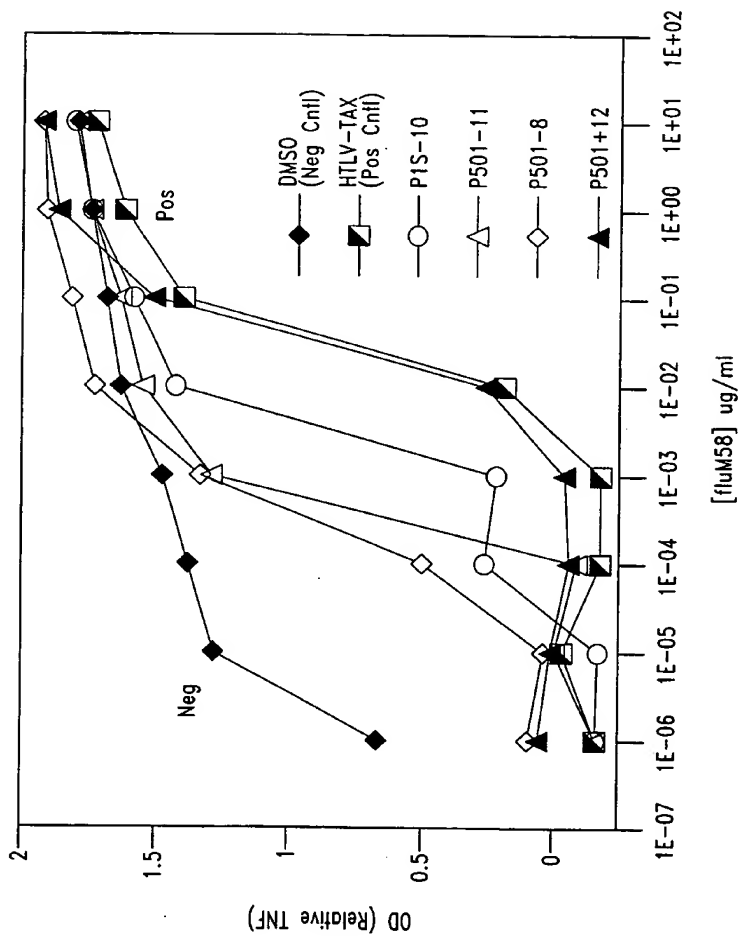
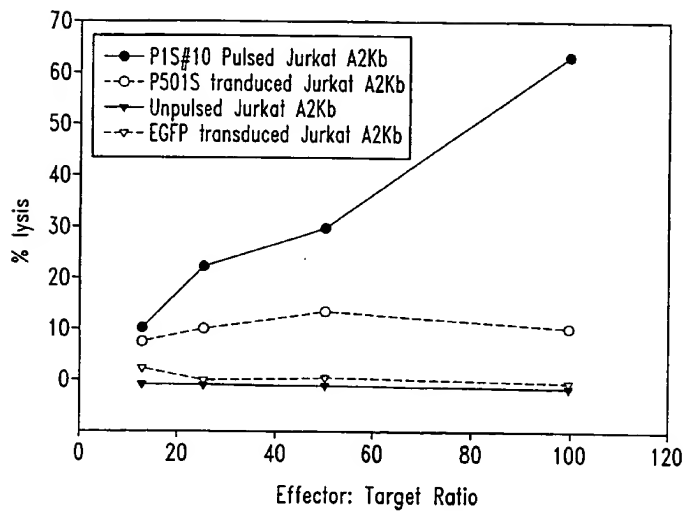
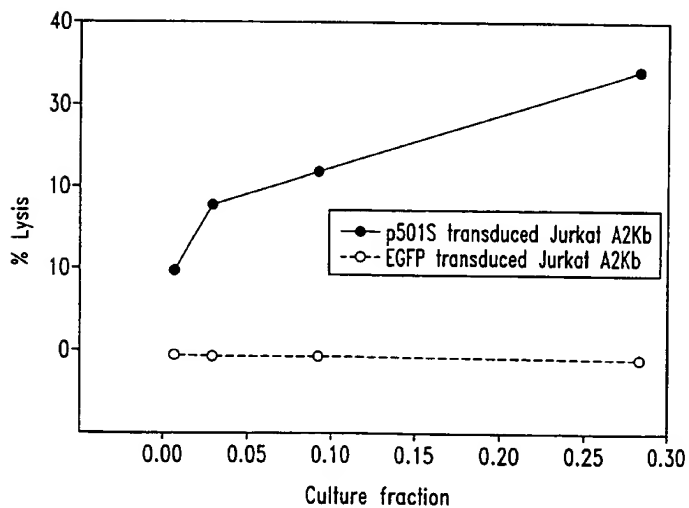


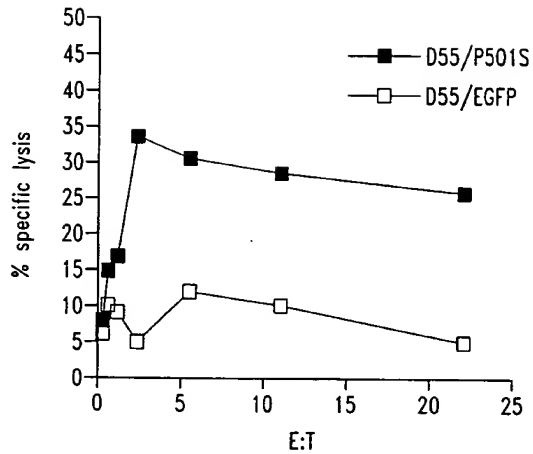
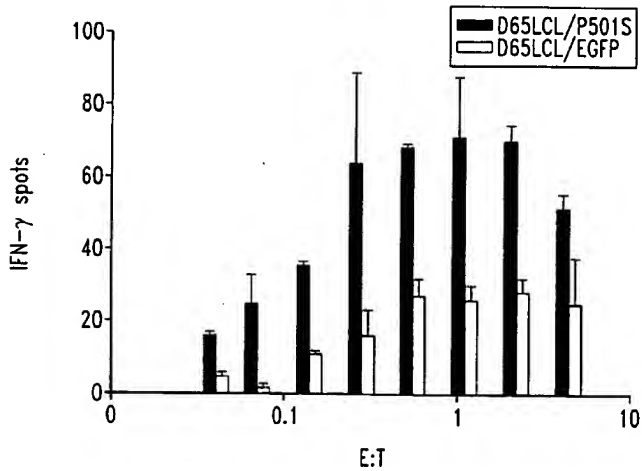
Fig. 3



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*Fig. 4**Fig. 5*

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*Fig. 6**Fig. 7*

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<213> Homo sapien

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<221> misc_feature
<222> (1) ... (773)
<223> n = A,T,C or G

```

```

<400> 3
cttttgaaag aagggtggc tgggtgttt aacagcagag gtgcagggcg ggggctcacg 60
tcttgcctct cactggtgat aaacgagccc cgttccttgt tgtgatcatg atgaacaacc 120
tctcaaaaag tcagaaccgg agtcacacag gcatctgtgc cgtcaaaagt ttgacaccac 180
tctgccttcg tcttctttgc aaatacatct gcaaaacttct tcttcatctc tggccaatca 240
tccatgtcca tctgattggg aagttcatca gactttagtc canmtccttt gatcagcagc 300
tcgtagaact ggggttctat tgctccaaca gccatgaatt ccccatctgc tgtcctgtaa 360
gtcgtataga aagggtgctc accatccaac atgttctgtc ctgcaggggg gggccgggtac 420
ccaattcgcc ctatantgag tcgtattacg cgcgctcact ggccgtcgtt ttacaacgctc 480
gtgactggga aaaccctggg cgttaccaac ttaatcgctt tgcagacat ccccttttcg 540
ccagctgggc gtaatanaga aaaggcccg cccgatcgcc cttccaacag ttgcgcacct 600
gaatgggnaa atgggacccc cctgttacg cgcattnaac ccccgcnagg tttngttgtt 660
acccccacnt nnaccgctta cactttgccg gcgccttanc gcccgctccc tttcnccttt 720
cttcccttcc tttcncncn ctttcccccg ggggttcccc cntcaaaccc cna 773

```

```

<210> 4
<211> 828
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (828)
<223> n = A,T,C or G

```

```

<400> 4
cctcctgagt cctactgacc tgtgctttct ggtgtggagt ccagggtctg taggaaaagg 60
aatgggcaga cacaggtgta tgccaatgtt tctgaaatgg gtataatttc gtcctctcct 120
tcggaacact ggctgtctct gaagacttct cgctcagttt cagttagggc acacacaaag 180
acgtgggtga ccatgttgtt tgtgggtgac agagatggga ggggtggggc ccaccctgga 240
agagtggaca gtgacacaag gtggacactc tctacagatc actgaggata agctggagcc 300
acaatgcatg aggcacacac acagcaagga tgacnctgta aacatagccc acgctgtcct 360

```

```

gngggcactg ggaagcctan atnaggccgt gagcanaaag aaggggagga tccactagtt 420
ctanagcgcc cgcaccgcgt gtgganctcc ancttttggt cctcttagtg aggggttaatt 480
gcgcgcttgg cntaatcatg gtcatanctn tttcctgtgt gaaattgtta tccgctcaca 540
attccacaca acatacganc cggaaacata aantgtaaac ctggggtgcc taatgantga 600
ctaactcaca ttaattgcgt tgcgctcact gcccgcttcc caatcnggaa acctgtcttg 660
ccncttgcat tnatgaatcn gccaaccccc ggggaaaagc gtttgcgttt tgggcgctct 720
tccgcttcc cncctcantta ntccctncnc tcggtcattc cggtcgngc aaaccggttc 780
accnctcca aaggggggat tccggtttcc ccnaatccgg gganance 828

```

&lt;210&gt; 5

&lt;211&gt; 834

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (834)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 5

```

ttttttttt tttttactga tagatggaat ttattaagct tttcacatgt gatagcacat 60
agttttaatt gcatccaaag tactaacaaa aactctagca atcaagaatg gcagcatggt 120
attttataac aatcaacacc tgtggctttt aaaatttggg tttcataaga taattttatac 180
tgaagtaaat ctaggcctgc ttttaaaaaa tgctttaggt cactccaagc ttggcagtta 240
acatttgcca taaacaataa taaaacaatc acaatttaat aaataacaaa tacaacattg 300
taggccataa tcatatacag tataaggaaa aggtggtagt gttgagtaag cagtatttag 360
aatagaatac cttggcctct atgcaaatat gtctagacac ttgattcac tcagccctga 420
cattcagttt tcaaagtagg agacagggtc tacagtatca ttttacagtt tccaacacat 480
tgaaaaacag tagaaaaatga tgagttgatt ttattaatg cattacatcc tcaagagtta 540
tcaccaaccc ctccagtata aaaaattttc aagttatatt agtcatataa cttggtgtgc 600
ttattttaaa ttagtgctaa atggattaag tgaagacaac aatgggtccc taatgtgatt 660
gatattgggc atttttaccg gcttctaata ctnaactttc aggcttttga actggaacat 720
tgnatnacag tgttccanag ttncaccta ctggaacatt acagtgtgct tgattcaaaa 780
tgttattttg ttaaaaaatta aattttaacc tggtggaata ataatttgaa atna 834

```

&lt;210&gt; 6

&lt;211&gt; 818

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (818)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 6

```

ttttttttt tttttttttt aagaccctca tcaatagatg gagacataca gaaatagtca 60
aaccacatct aaaaatggc agtatcaggc ggcggcttcg aagccaaagt gatgtttgga 120
tgtaaaagtga aatattagtt ggcggatgaa gcagatagtg aggaaagtg agccaataat 180
gacgtgaagt ccgtggaagc ctgtggctac aaaaaatgtt gagccgtaga tgcgctcgga 240
aatgggtaag ggagactcga agtactctga ggcttgtagg agggtaaaat agagaccag 300
taaaattgta ataagcagtg cttgaattat ttggtttcgg ttgttttcta ttagactatg 360
gtgagctcag gtgattgata ctctgatgc gagtaatacg gatgtgttta ggaaggggac 420
ttctagggga tttagcgggg tgatgcctgt tgggggccag tgcctccta gttggggggt 480
aggggctagg ctggagtggc aaaaggctca gaaaaatcct gcgaagaaaa aaacttctga 540

```

```

ggtaataaat aggattatcc cgtatcgaag gcctttttgg acaggtggtg tgtggtggcc 600
ttggtatgtg ctttctcgtg ttacatcgcg ccattcattgg tatatgggta gtgtgttggg 660
ttantanggc ctantatgaa gaacttttgg antggaatta aatcaatngc ttggccggaa 720
gtcattanga nggctnaaaa ggccttgta ngggtctggg ctnggtttta cccnaccat 780
ggaatncnc ccccggaacna ntgnatccct attcttaa 818

```

```

<210> 7
<211> 817
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (817)
<223> n = A,T,C or G

```

```

<400> 7
tttttttttt tttttttttt tggtcttaga gggggttagag ggggtgctat agggtaaata 60
cgggccctat ttcaaagatt tttaggggaa ttaattctag gacgatgggt atgaaactgt 120
ggtttgtctc acagatttca gagcattgac cgtagtatac ccccggtcgt gtgacgggtga 180
aagtgggttg gtttagacgt ccgggaattg catctgtttt taagccta atgtgggacag 240
ctcatgagtg caagacgtct tgtgatgtaa ttattatacn aatgggggct tcaatcgga 300
gtactactcg attgtcaacg tcaaggagtc gcaggtcgcc tggttctagg aataatgggg 360
gaagtatgta ggaattgaag attaatccgc cgtagtcggt gttctcctag gttcaatacc 420
attggtggcc aattgatttg atggtaaggg gagggatcgt tgaactcgtc tggttatgtaa 480
aggatncctt ngggatggga aggcnatnaa ggactangga tnaatggcgg gcangatatt 540
tcaaacngtc tctantctct gaaacgtctg aaatgttaat aanaattaaan ttntgttatt 600
gaatnttnng gaaaagggtc tacaggacta gaaaccaa atnntaangg 660
cnttatcntn aaaggtnata accnctccta tnatcccacc caatngnatt cccacnncnn 720
acnattggat nccccanttc canaaanggc cnccccccg tgnannccnc cttttgttcc 780
cttnantgan ggttattcnc cctnngcctt atcance 817

```

```

<210> 8
<211> 799
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (799)
<223> n = A,T,C or G

```

```

<400> 8
catttcgggg tttactttct aaggaaagcc gagcggaagc tgctaactgt ggaatcggtg 60
cataaggaga actttctgct ggcacgcgct agggacaagc gggagagcga ctccgagcgt 120
ctgaagcgca cgtcccagaa ggtggacttg gcactgaaac agctgggaca catccgcgag 180
tacgaacagc gcctgaaagt gctggagcgg gaggtccagc agtgtagccg cgtctctggg 240
tgggtggccg angcctganc cgctctgcct tgcgtccccc angtgggccg ccacccctcg 300
acctgcctgg gtccaaacac tgagccctgc tggcggactt caagganaac cccacangg 360
ggattttgct cctanantaa ggctcatctg ggccctcgcc cccccacctg gttggccttg 420
tccttgangt gagccccatg tccatctggg ccaactgtcng gaccaccttt ngggagtgtt 480
ctccttacia ccacannatg cccggctcct cccggaaacc antccancc tnggaaggat 540
caagnccctg atccactnnt nctanaaccg gccnccnccg cngtggaacc cnccttntgt 600
tccttttnt tnaagggtta tnnccgcttg gccttnccan ngctctncnc nttttccnnt 660
gttnaaattg ttangcnccc nccnntcccn cnnnnnnan cccgaccenn annttnnann 720

```

```
nccctgggggt nccnnncgat tgaccenncc nccctntant tgcnttnggg ncnntngccc 780
ctttccctct nggganncg 799
```

```
<210> 9
<211> 801
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (801)
<223> n = A,T,C or G
```

```
<400> 9
acgccttgat cctcccaggc tgggactggt tctgggagga gccgggcatg ctgtgggttg 60
taangatgac actcccaaaag gtggtcctga cagtggccca gatggacatg gggctcacct 120
caaggacaag gccaccagggt gcggggggccg aagcccacat gatccttact ctatgagcaa 180
aatcccctgt gggggcttct ccttgaagtc cgccancagg gctcagtctt tggacccang 240
caggtcatgg ggttgtngnc caactggggg ccncaacgca aaanggcnc aaggcctcngn 300
caccatcccc angacgcggc tacactnctg gacctcccnc tccaccactt tcatgcgctg 360
ttcntaccgg cgnatntgtc ccactgttt cngtgccnac tccancttct nggacgtgcg 420
ctacatacgc cgggancnc nctcccgtt tgtccctatc cacgtncan caacaaattt 480
cncntantg caccnattcc cacttttnc agntttcnc nncngcttc cttntaaaag 540
ggttgancgc cggaaaatnc cccaaaaggg gggggccngg tacccaactn cccctnata 600
gctgaantcc ccatnaccnn gnctnatgg anccntccnt ttttaannacn ttctnaactt 660
gggaanancc ctgncnctn ccccnnttaa tccnccttg cnangnnct ccccnntcc 720
nccnnntng gcntntnann cnaaaaaggc ccnnancaa tctcctnnn cctcanttgc 780
ccanccctcg aaatcgccn c
```

```
<210> 10
<211> 789
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (789)
<223> n = A,T,C or G
```

```
<400> 10
cagtctatnt gccagtggtg gcagctttcc ctgtggctgc cggtgccaca tgctgtccc 60
acagtggtggc cgtggtgaca gcttcagccg ccctcaccgg gtccaccttc tcagccctgc 120
agatcctgcc ctacacactg gcctcccctc accaccggga gaagcaggtg ttctgtccca 180
aataccgagg ggacactgga ggtgctagca gtgaggacag cctgatgacc agcttctctg 240
caggccctaa gcctggagct cccttcccta atggacacgt ggggtctgga ggcagtgccc 300
tgctcccacc tccaccgcg ctctgcgggg cctctgcctg tgatgtctcc gtacgtgtgg 360
tggtgggtga gcccaccgan gccaggggtg ttccggggccg gggcatctgc ctggacctgc 420
ccatcctgga tagtgcttcc tgctgtccca ngtggcccca tccctgttta tgggctccat 480
tgtccagctc agccagtgct tcaactgccta tatggtgtct gccgcaggcc tgggtctggt 540
cccatttact ttgctacaca ggtantattt gacaagaacg anttggccaa atactcagcg 600
ttaaaaaaat ccagcaacat tgggggtgga aggcctgcct cactgggtcc aactccccgc 660
tcctgttaac cccatggggc gcccggttg gccgccaatt tctgtgtctg ccaaantnat 720
gtggctctct gctgccacct gttgtggct gaagtgcnta cngcncant nggggggtng 780
gnggttccc
```

<210> 11  
 <211> 772  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(772)  
 <223> n = A,T,C or G

<400> 11  
 cccaccctac ccaaatatta gacaccaaca cagaaaagct agcaatggat tcccttctac 60  
 tttgttaaat aaataagtta aatatatttaa tgcctgtgtc tctgtgatgg caacagaagg 120  
 accaacaggc cacatcctga taaaaggtaa gaggggggtg gatcagcaaa aagacagtgc 180  
 tgtgggtcga ggggacctgg ttcttgtgtg ttgccctca ggactcttcc cctacaaata 240  
 actttcatat gttcaaatcc catggaggag tgtttcatcc tagaaactcc catgcaagag 300  
 ctacattaaa cgaagctgca gggttaagggg cttanagatg ggaaaccagg tgactgagtt 360  
 tattcagctc ccaaaaaccc ttctctaggt gtgtctcaac taggagggcta gctgttaacc 420  
 ctgagctcgg gtaatccacc tgcagagtcc ccgcattcca gtgcatggaa cccttctggc 480  
 ctccctgtat aagtccagac tgaaaccccc ttggaaggnc tccagtcagg cagccctana 540  
 aactggggaa aaaagaaaag gacgccccan cccccagctg tgcantcagc cacctcaaca 600  
 gcacagggtg gcagcaaaaa aaccacttta ctttggcaca aacaaaaact ngggggggca 660  
 accccggcac cccnangggg gttaacagga ancngggnaa cntggaaccc aattnaggca 720  
 ggcccnccac cccnaatntt gctgggaaat ttttctctcc ctataatntt tc 772

<210> 12  
 <211> 751  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(751)  
 <223> n = A,T,C or G

<400> 12  
 gcccgaattc cagctgccac accaccacag gtgactgcat tagttcggat gtcatacaaa 60  
 agctgattga agcaaccctc tacttttttg tctgtgagct tttgcttggg gcaggtttca 120  
 ttggctgtgt tgggtgacgtt gtcattgcaa cagaatgggg gaaaggcact gttctctttg 180  
 aagtanggtg agtcctcaaa atccgtatag ttggtgaagc cacagcactt gagccctttc 240  
 atggtgggtg tccacacttg agtgaagtct tcctgggaac cataatcttt ctgtatggca 300  
 ggcactacca gcaacgtcag ggaagtgtct agccattgtg gtgtacacca aggcgaccac 360  
 agcagctgcn acctcagcaa tgaagatgan gaggangatg aagaagaacg tcncgagggc 420  
 acactgtctc tcagctcttan caccatanca gcccntgaaa accaananca aagaccacna 480  
 cncgcgctgc gatgaagaaa tnaccccneg ttgacaaact tgcattggac tggganccac 540  
 agtggccena aaaaatcttca aaaaggatgc cccatcnatt gaccccccaa atgcccactg 600  
 ccaacagggg ctgccccacn cncnnaacga tgancnatt gnacaagatc tncntggctc 660  
 tnatnaacnt gaacctgtcn tngtggctcc tgttcaggnc cnnngcctga cttctnaann 720  
 aangaactcn gaagncacca cngganannn g 751

<210> 13  
 <211> 729  
 <212> DNA  
 <213> Homo sapien



<220>  
 <221> misc\_feature  
 <222> (1)...(729)  
 <223> n = A,T,C or G

<400> 13  
 gagccaggcg tccctctgcc tgccactca gtggcaacac ccgggagctg ttttgcctt 60  
 tgtggancct cagcagtncc ctctttcaga actcantgcc aagancctcg aacaggagcc 120  
 accatgcagt gcttcagctt cattaagacc atgatgatcc tcttcaattt gctcatcttt 180  
 ctgtgtggtg cagccctggt ggcagtgggc atctgggtgt caatcgatgg ggcatccttt 240  
 ctgaagatct tcgggccact gtcgtccagt gccatgcagt ttgtcaacgt gggctacttc 300  
 ctcatcgtag ccggcggtgt ggtcttagct ctagggttcc tgggctgcta tgggtgctaag 360  
 actgagagca agtgtgccct cgtgacgttc ttcttcatcc tcctcctcat ctccattgct 420  
 gaggttgcaa tgctgtggtc gccttggtgt acaccacaat ggctgagcac ttcctgacgt 480  
 tgctggtaat gcctgccatc aanaaaagat tatgggttcc caggaanact tcactcaagt 540  
 gttggaacac caccatgaaa gggctcaagt gctgtggctt cnnccaacta tacggatttt 600  
 gaagantcac ctacttcaaa gaaaanagt cctttccccc atttctgttg caattgacaa 660  
 acgtccccaa cacagccaat tgaaaacctg caccacaacc aaangggctc ccaaccanaa 720  
 attnaaggg 729

<210> 14  
 <211> 816  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(816)  
 <223> n = A,T,C or G

<400> 14  
 tgctcttctt caaagttggt cttgttgcca taacaaccac cataggtaaa gcggggcgag 60  
 tgttcgctga aggggttgta gtaccagcgc gggatgctct ccttgacagag tcctgtgtct 120  
 ggcaggtcca cgcagtgcc tttgtcactg gggaaatgga tgcgctggag ctcgtaaaag 180  
 ccaactcgtg atttttcaca ggcagcctcg tccgacgcgt cggggcagtt ggggggtgtct 240  
 tcacactcca ggaaactgtc natgcagcag ccattgtgc agcggaaactg ggtgggctga 300  
 cangtgccag agcacactgg atggcgctt tccatgnnan gggccctgng ggaagtcctc 360  
 tgancccan anctgcctct caaangcccc accttgaca ccccgacagg ctagaatgga 420  
 atcttcttcc cgaaaggtag ttnttcttgt tgcccaancc anccccntaa acaaactctt 480  
 gcanatctgc tccngggggg tcntantacc ancggtggaa aagaacccca ggcnegcaac 540  
 caancttgtt tggatncgaa gcnataatct nctnttctgc ttggtggaca gcaccantna 600  
 ctgtnnanc ttagncctntg gtcctcnttg gtggncttg aacctaatcn ccnntcaact 660  
 gggacaaggt aantngcct cctttnaatt cccnancntn cccctggtt tgggggtttt 720  
 cncnctcta cccagaaaan nccgtgttcc ccccaacta ggggcnnaa ccnntnttc 780  
 cacaaccctn ccccaaccac ggggtcngnt ggttng 816

<210> 15  
 <211> 783  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(783)  
 <223> n = A,T,C or G

```

<400> 15
ccaaggcctg ggcaggcata nacttgaagg tacaacccca ggaacccctg gtgctgaagg      60
atgtggaaaa cacagattgg cgccactgac ggggtgacac ggatgtcagg gtagagagga      120
aagacccaaa ccaggtggaa ctgtggggac tcaaggaang cacctacctg ttccagctga      180
cagtgactag ctcagaccac ccagaggaca cggccaacgt cacagtcact gtgctgtcca      240
ccaagcagac agaagactac tgcctcgcat ccaacaangt gggctgctgc cggggctctt      300
tcccacgctg gtactatgac cccacggagc agatctgcaa gagtttcgtt tatggaggct      360
gcttgggcaa caagaacaac taccttcggg aagaagagtg cattctancc tgtcnggggt      420
tgcaaggctg gcctttgana ngcanctctg gggctcangc gactttcccc cagggccctt      480
ccatggaaag gcgccatcca ntgttctctg gcacctgtca gcccaccagg ttccgctgca      540
ncaatggctg ctgcatcnac antttcctng aattgtgaca acacccccca ntgcccccaa      600
ccctcccaac aaagcttccc tgttnaaaaa tacnccantt ggcttttnac aaacnccggg      660
cncttcnntt tccccnntn aacaaagggc nctngcnttt gaactgcccn aaccnnggaa      720
tctnccnngg aaaaantncc cccctgggtt cctnnaancc cctcncnnaa anctncccc      780
ccc                                                                                   843

```

```

<210> 16
<211> 801
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(801)
<223> n = A,T,C or G

```

```

<400> 16
gccccaatcc cagctgccac accaccacag gtgactgcat tagttcggat gtcatacaaa      60
agctgattga agcaaccctc tacttttttg tcgtgagcct tttgcttggg gcagggtttca      120
ttggctgtgt tgggtgacgtt gtcattgcaa cagaatgggg gaaaggcact gttctctttg      180
aagttaggggt agtccctcaa atccgtatag ttggtgaagc cacagcactt gagccctttc      240
atggtgggtg tccacacttg agtgaagctc tcctgggaac cataatcttt ctgtatggca      300
ggcactacca gcaacgtcag gaagtgtcca gccattgtgg tgtacaccaa ggcgaccaca      360
gcagctgcaa cctcagcaat gaagatgagg aggaggatga agaagaacgt cncgagggca      420
cacttgctct ccgtcttagc accatagcag cccangaaac caagagcaaa gaccacaacg      480
ccngctgcga atgaaagaaa ntacccacgt tgacaaactg catgggccct ggacgcacgt      540
tggcccgaan atcttcagaa aagggatgcc ccacgattg aacaccana tgcccactgc      600
cnacagggct gcncncncn gaaagaatga gccattgaag aaggatcctc ntggctctta      660
tgaactgaaa ccntgcatgg tggcccctgt tcagggtctc tggcagtgaa ttctganaaa      720
aaggaacngc ntnagcccc ccaaangana aaacaccccc ggggtgttgc ctgaattggc      780
ggccaaggan ccctgccccn g                                                                                   801

```

```

<210> 17
<211> 740
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(740)
<223> n = A,T,C or G

```

```

<400> 17
gtgagagcca ggcgtccctc tgcctgcccc ctcaaggcca acaccggga gctgttttgt      60

```

```

cctttgtgga gcctcagcag ttcctctctt cagaactcac tgccaagagc cctgaacagg 120
agccaccatg cagtgcctta gcttcattaa gaccatgatg atcctcttca atttgcctcat 180
ctttctgtgt ggtgcagccc tgttggcagt gggcatcttg gtgtcaatcg atggggcatc 240
ctttctgaag atcttcgggc cactgtcgtc cagtgccatg cagtttgtca acgtgggcta 300
cttcctcacc gcagccggcg ttgtggctct tgcctcttgg ttcctgggct gctatgggtg 360
taagacggag agcaagtgtg ccctcgtgac gttcttcttc atcctcctcc tcatcttcat 420
tgctgaagtt gcagctgctg tggtcgcctt ggtgtacacc acaatggctg aaccattcct 480
gacgttgcctg gtantgcctg ccctcaanaa agattatggg ttcccaggaa aaattcactc 540
aantntggaa caccnccatg aaaagggctc caatttctgn tggcttcccc aactataccg 600
gaattttgaa agantcnccc tacttccaaa aaaaaanant tgcctttncc cccttctctg 660
tgcaatgaaa acntcccaan acngccaatn aaaacctgcc cnnncaaaaa ggntcncaaa 720
caaaaaaant nnaaggggtn 740

```

```

<210> 18
<211> 802
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(802)
<223> n = A,T,C or G

```

```

<400> 18
ccgctgggtg cgctgggtcca gngnagccac gaagcacgtc agcatcacaca gcctcaatca 60
caaggtcttc cagctgccgc acattacgca gggcaagagc ctccagcaac actgcatatg 120
ggatacactt tactttagca gccaggggtga caactgagag gtgtcgaagc ttattcttct 180
gagcctctgt tagtggagga agattccggg cttcagctaa gtatgcagcg tatgtcccat 240
aagcaaacac tgtgagcagc cggaaagtag aggcmaaagc actctcagcc agctctctaa 300
cattgggcat gtccagcagt tctccaaaca cgtagacacc agnggctctc agcacctgat 360
ggatgagtgt ggccagcgct gcccccttgg ccgacttggc taggagcaga aattgctcct 420
ggttctgccc tgtcaccttc acttccgcac tcatcactgc actgagtgtg ggggacttgg 480
gctcaggatg tccagagacg tggttccgcc ccctcnctta atgacaccgn ccanncaacc 540
gtcggctccc gccgantgng ttcgtcgtnc ctgggtcagg gtctcgtggc cncactttgc 600
aancttctgc nggccccatg aattcacenc accggaactn gtangatcca ctntttctat 660
aaccgngnyc caccgcnntt ggaactccac tcttntncc ttactctgag ggttaaggtc 720
acccttnncg ttactcttgg ccaaaccntn cntgtgtcgc anantgtnaa tcngngncca 780
tnccancnc atangaagcc ng 802

```

```

<210> 19
<211> 731
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(731)
<223> n = A,T,C or G

```

```

<400> 19
cnaagcttcc aggtnacggg ccgcnancc tgaccnagg tancanaang cagnncgagg 60
gagccaccg tcacgngngn gngtctttat nggagggggc ggagccacat cncctggacnt 120
cmtgacccca actcccncnc ncnantgca gtgatgagtg cagaactgaa ggtnacgtgg 180
caggaaccaa gancaaannc tgctccnttc caagtcggcn nagggggcgg ggctggccac 240
gcncatcct cnagtgtcgn aaagcccn cctgtctact tgtttggaga acngcnnga 300

```

```

catgcccagn gttanataac nggcngagag tnannttgcc tctcccttcc ggctgcgcan 360
cngntgtgct tagngggacat aacctgacta cttaaactgaa cccnngaate tncnccccct 420
ccactaagct cagaacaaaa aacttcgaca ccactcantt gtcacctgnc tgctcaagta 480
aagtgtacct catncccaat gntgctnga ngctctgncc tgcnttangt tcggctctgg 540
gaagacctat caattnaagc tatgtttctg actgctctct gctccctgna acaancnacc 600
cnnccntcca aggggggggnc ggcccccaat ccccccaacc ntnaattnan ttancccccn 660
ccccngggcc ggccctttta cnancntcnn nnacnnggna aaacennngc tttncccaac 720
nnaatecncc t 731

```

<210> 20

<211> 754

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(754)

<223> n = A,T,C or G

<400> 20

```

tttttttttt tttttttttt taaaaacccc ctccattnaa tgnaaacttc cgaaattgtc 60
caacccccct ntccaaatnn ccttttccgg gnggggggttc caaacccaan ttannttttg 120
annttaaat aaatnttntt tggnggnnna anccnaatgt nangaaagtt naaccanta 180
tnancctnaa tncctggaaa cngtngntt ccaaaaatnt ttaaccctta antccctccg 240
aaatngttna nggaaaaacc aantttctnt aaggttggtt gaaggntnaa tnaaaanccc 300
nnccaattgt tttngccac gctgaatta attgnttcc gntgttttcc nttaaaanaa 360
ggnnancccc ggttantnaa tcccccnnc cccaattata ccganttttt ttngaattgg 420
ganccnccgg gaattaacgg ggnnnntccc tnttgggggg cnggnncccc cccctcggg 480
ggttngggnc aggnccnaat tgtttaaggg tccgaaaaat ccctccnaga aaaaaanctc 540
ccaggnatgag nntnggggtt ncccccccc cangggccct ctcgnanagt tgggggtttg 600
ggggcctggg attttnttcc cctntttnc tcccccccc cngggganag aggttngngt 660
ttgtntcnnn ggccccnccn aaganccttn ccganttnan ttaaatccnt gcctnnggca 720
agtccnttgn agggntaaan ggccccctnn cggg 754

```

<210> 21

<211> 755

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(755)

<223> n = A,T,C or G

<400> 21

```

atcancccat gaccccaaac nngggaccnc tcancgggnc nnncnaccnc cggccnatca 60
nngtnagnnc actnccntnn natcacnccc cncnactac gcccnananc cnacgcncta 120
nncanatncc actganngcg cgangtngan ngagaaanct nataccanag ncaccanacn 180
ccagctgtcc nanaangcct nnnatacnng nnnatccaat ntgnanccct cnaagtattt 240
nnccnccat gattttctn anccgattac cctncccccc tancctctcc cccccacna 300
cgaaggcnct ggnccnaagg nngcgnccnc cgcgtagntc cccnccaagt cncnccncta 360
aactcancn nattaacncc ttctntgagta tcaactcccg aatctcaccc tactcaactc 420
aaaaanacn gatacaaat aatncaagcc tgnttatnac actntgactg ggtctctatt 480
ttagnngtcc ntnaancntc ctaatacttc cagtctncc tcnccaattt cnaanggct 540
ctttcnagca gcatnttttg gttcccnntt ggggtcttan ngaattgcc tctntngaac 600

```

```

gggctctctct tttccttcgg ttancctggn ttcnncgggc cagttattat tttccntttt 660
aaattctntnc cntttanttt tggcnttcna aacccccggc cttgaaaacg gccccctggg 720
aaaaggttgc tttganaaaa tttttgtttt gtccc 755

```

<210> 22

<211> 849

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(849)

<223> n = A,T,C or G

<400> 22

```

tttttttttt tttttangtg tngtcgtgca ggtagaggct tactacaant gtgaanacgt 60
acgctnngan taangcgacc cgantttctag gannncacct aaaatcanac tgtgaagatn 120
atcctgnnaa cggaaangtc accggnngat nntgctaggg tgnccnctcc cannncttn 180
cataactcng nggccttgcc caccaccttc ggcggcceng ngcccgggcc cgggtcattn 240
gnnttaacn cactnngcna ncgggttccn nccccnncng acccnggcga tccgggggtnc 300
tctgtcttcc cctgnagncn aaaaantggg ccnccggccc ctttaccctt nnacaagcca 360
cngccttcta nccnccgccc cccctccant nngggggact gccnannget ccgttctnng 420
nnaccccnnn gggttcctcg gttgtcgant cnaccgnang ccanggattc cnaaggaagg 480
tgcgttnttg gccctacccc ttcgctnccg nncacccttc ccgacnanga nccgctcccc 540
cncnccgnng cctcncctcg caacacccgc nctctctngt ncggnnnccc ccccaccgc 600
nccctcncnc ngncgnannc ctcnccnccc gtctcanna ccaccccgcc ccgccaggcc 660
ntcancaen ggnngacnng naccnccntc gcncgcgcgn gcgncnccct cgcncngaa 720
ctnctcngg ccantnncgc tcaanccnna cnaaacgccg ctgcgcggcg cgnagcgncc 780
ncctcncga gtcctcccg nctccncccc angnnttccn cgaggacacn nnaccccgcc 840
nncangcgg 849

```

<210> 23

<211> 872

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(872)

<223> n = A,T,C or G

<400> 23

```

gcgcaaaacta tacttcgctc gnactcgtgc gcctcgtcnc tcttttcctc cgcaaccatg 60
tctgacnanc ccgattnggc ngatatcnan aagntcganc agtccaaact gantaacaca 120
cacacncnan aganaaatcc nctgccttcc anagtanacn attgaacnng agaaccangc 180
nggcgaatcg taatnaggcg tgcgcgcgca atntgtcncc gtttattntn ccagctcnc 240
ctnccncccc tacttcttcn nagctgtcnn acccctngtn cgnacccccc naggtcggga 300
tcgggttttn nntgaccgng cnnccctcc cccntccat nacganccnc ccgaccacc 360
nanngcncgc nccccgnnct ctctgcncnc cctgtccttn cccctgtngc ctggcncngn 420
accgcattga ccctcgcnnc ctncnngaaa ncgnanacgt ccgggttggn annancgctg 480
tggggnngcg tctgcncgcg gttccttccn ncncttcca ccattctct tacnggggtc 540
cncgcctc tcnnncacnc cctgggacgc tntcctntgc ccccttnac tccccccct 600
cgnctgtncc cgncccccac ntcatttnca nacgntcttc acaannncc ggntnnctcc 660
cnancngcn gtcancncag ggaaggngg ggnnccnng nttgacgttg ngngngangtc 720
cgaan=ntcc tcncntcan cncatccct cgggcgnnct ctngttncc aacttancaa 780

```

ntctccccc ngngcncntc tcagcctcnc cccccccnt ctctgcantg tnetctgctc 840  
tnaccnntac gantnttcgn cneccctcttt cc 872

<210> 24

<211> 815

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(815)

<223> n = A,T,C or G

<400> 24

gcacgcaagc	ttgagtattc	tatagngtca	cctaaatanc	ttggcncat	catggctcna	60
nctgnccttc	tgtgtcaaat	gtatacnaa	tanatatgaa	tctnatntga	caagannnga	120
tcntncatta	gtaacaantg	tnntgtccat	cctgtcngan	canattccca	tnnattncgn	180
cgcatcncn	gcncantatn	taatngggaa	ntcnntnnn	ncaccnncat	ctatcntncc	240
gcncctgac	tggnagagat	ggatnanttc	tnntntgacc	nacatgttca	tcttggattn	300
aanancccc	cgcnngccac	cggttngnng	cnagccnntc	ccaagacctc	ctgtggaggt	360
aacctgcgtc	aganncatca	aacntgggaa	acccgcnncc	angtnnaagt	ngnnncanan	420
gateccgtcc	aggnntnacc	atcccttcnc	agcgccccct	ttngtgcctt	anagnnagc	480
gtgtccnanc	cnctcaacat	ganacgcgcc	agnccanccg	caatnnggca	caatgtcgnc	540
gaacccccct	gggggantna	tncaaanccc	caggattgtc	cnncnangaa	atcccnanc	600
ccnccctac	cnncctttgg	gacngtgacc	aantcccga	gtncagctcc	ggccngnctc	660
ccccaccggt	nncntgggg	gggtgaanct	cngnntcanc	cngncgaggn	ntcgnaagga	720
accggnctn	ggncgaanng	ancnntcnga	agnccnntc	cgtataaccc	ccctcncca	780
nccnncngnt	agntcccccc	cngggtncgg	aangg			815

<210> 25

<211> 775

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(775)

<223> n = A,T,C or G

<400> 25

ccgagatgtc	tcgctccgtg	gccttagctg	tgtctcgctc	actctctctt	tctggcctgg	60
aggctatcca	gcgtactcca	aagattcagg	tttactcacg	tcattccagca	gagaatggaa	120
agtcaaaatt	cctgaattgc	tatgtgtctg	ggtttcatcc	atccgacatt	gaanttgact	180
tactgaagaa	tgganagaga	attgaaaaag	tggagcattc	agacttgtct	ttcagcaagg	240
actgtctctt	ctatctcntg	tactacactg	aattcaccoc	cactgaaaaa	gatgagtatg	300
cctgcccgtg	gaaccatgtg	actttgtcac	agcccaagat	agttaaagtg	gatcgagaca	360
tgtaaagcag	cnncatggaa	gtttgaagat	gccgcatttg	gattggatga	attccaaatt	420
ctgcttgctt	gcnttttaat	antgatatgc	ntatacaccc	taccttttat	gnccccaaat	480
tgtagggggt	acatnantgt	tcnctnngga	catgatcttc	ctttataant	ccnccnttcg	540
aattgcccgt	cncccngttn	ngaattgttc	cnnaaccacg	gttggctccc	ccaggtcncc	600
tcttacggaa	gggcctgggc	cnctttncaa	gggtggggga	accnaaaatt	tcnctnttgc	660
ccncccncca	cnntcttgng	nncncanttt	ggaacccttc	cnattccctc	tggcctcnna	720
nccttnncta	anaaaacttn	aaancgtngc	naaanntttn	acttcccccc	ttacc	775

<210> 26

<211> 820  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(820)  
 <223> n = A,T,C or G

<400> 26  
 anattantac agtgtaatct tttcccagag gtgtgtanag ggaacggggc ctagaggcat 60  
 cccanagata ncttatanca acagtgcctt gaccaagagc tgctgggcac atttcttgca 120  
 gaaaagggtg cggtcccat cactcctcct ctcccatagc catcccagag gggtgagtag 180  
 ccatcangcc ttcggtggga gggagtcang gaaacaacan accacagagc anacagacca 240  
 ntgatgacca tgggcgggag cgagcctctt cctcgnaccg ggggtggcana nganagccta 300  
 nctgaggggt cacactataa acgttaacga ccnagatnan cacctgcttc aagtgcaccc 360  
 ttctacctg acnaccagng accnnnaact gcngcctggg gacagcctg ggancagcta 420  
 acnnagcact cacctgcccc cccatggcgg tncgcntccc tggctcctgnc aagggagct 480  
 cctgttgga attncgggga naccaaggga nccccctcct ccanctgtga aggaaaaann 540  
 gatggaaatt tnccttccg gccnntcccc tcttcttta caegccccct nntactctc 600  
 tccctctnt ntcctgncnc acttttnacc ccnnnatttc ccttnattga tcggannctn 660  
 ganattccac tncgcctcnc cntcncatng naanacnaaa nactntctna ccnggggat 720  
 gggnnccctg ntcctcctct ctttttctc accnccnnt ctttgctct ccttngatca 780  
 780tccaaacntc gntggccctn cccccccnnn tcttttncce  
 820

<210> 27  
 <211> 818  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(818)  
 <223> n = A,T,C or G

<400> 27  
 tctgggtgat ggctcttcc tctcaggga cctctgactg ctctgggcca aagaatctct 60  
 tgtttcttct ccgagcccca ggcagcgggt attcagccct gcccaacctg attctgatga 120  
 ctgaggatgc tgtgacggac ccaaggggca aatagggtcc cagggtccag ggaggggcgc 180  
 ctgctgagca cttccgcccc tcacctgccc cagccctgac catgagctct gggtgggtc 240  
 tccgctcca gggttctgct cttccangca ngccanacag tggcgctggg ccacactggc 300  
 ttcttctgccc cccntccctg gctctganc tctgtcttcc tgtcctgtgc angnccttg 360  
 gatctcagtt tccctcctc anngaactct gtttctgann tcttcantta actntgant 420  
 tatnaccnan tggncctgnc tgcnnactt taatgggccc gaccggctaa tccctccctc 480  
 nctcccttcc anttcnnna accngcttnc cntctctcc cntancccg ccnggggaanc 540  
 ctcccttgc ctnaccang gccnnnaccg cccntnnctn ggggggcnng gtntctncnc 600  
 ctgntnnccc cncctcncnt tncctcgccc cncnncgcn nngcannctc ncngtcccn 660  
 tnnctcttcn ngntcgnaa ngntcncntn tnnnnngcnc ngntntnctn tccctctcnc 720  
 cnnntgnang tnnntnnnc ncngnncccc nnnnnnnnn nggnntnnn tctncncngc 780  
 cccncccccc ngnattaagg cctccnntct ccggccnc 818

<210> 28  
 <211> 731  
 <212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(731)

<223> n = A,T,C or G

<400> 28

```

aggaagggcg gagggatatt gtangggatt gagggatagg agnataaangg gggaggtgtg      60
tcccaacatg anggtgnngt tctcttttga angaggggttg ngtttttann ccnggtgggt      120
gattnaaccc cattgtatgg agnnaaaagn tttnagggat ttttcggctc ttatcagtat      180
ntanattcct gtnaatcgga aaatnatntt tcnnncggaa aatnttgctc ccatccgnaa      240
attntccccc ggtagtgcac nttngggggg cngccangtt tcccaggctg ctanaatcgt      300
actaaagntt naagtgggan tncaaatgaa aacctnncac agagnatccn taccgcagctg      360
tnnnttcnct tcgccctntg actctgcnnng agcccaatac ccnngngnat gtcncccnng      420
nnngcgcncn tgaannnnnc tcngggcctnn gancatcang ggggttcgcga tcaaaagcnn      480
cgtttcncat naaggcactt tngcctcctc caaccnctng ccctcnncca tttngccgtc      540
nggttcnctc acgctnnntg cncctnnntn ganattttnc ccgcttnggg naancctcct      600
gnaatgggta gggncctntc ttttnaccnn gnggtntact aatcnnctnc acgctnctt      660
tctcnacccc cccccctttt caatccanc ggcnaatggg gtctcccnng cgangggggg      720
nnncccnnc c

```

<210> 29

<211> 822

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(822)

<223> n = A,T,C or G

<400> 29

```

actagtccag tgtggtggaa ttccattgtg ttggggncnc ttctatgant antnttagat      60
cgctcanacc tcacancctc ccnacnangc ctataangaa nannaataga nctgtncnnt      120
atntntacnc tcatanncct cnnnaccac tccctcttaa ccnctactgt gcctatngcn      180
tnnctantct ntgccgcctn cnanccaccn gtggggccnac cncnngnat ctcnatctcc      240
tcnccatntn gcctananta ngtnataacc ctatacctac nccaatgcta nnnctaancn      300
tccatnantt annntaacta ccactgacnt ngactttcnc atnanctcct aatttgaatc      360
tactctgact cccacngcct annnattagc anctccccc nacnatntct caaccaaatc      420
ntcaacaacc tatctantct ttncccaacc nttncctccg atccccnnac aacccccctc      480
ccaaataacc nccacttgac ncctaacccn caccatcccg gcaagccnan ggnattttan      540
ccactggaat cacnatngga naaaaaaac ccnaactctc tancncnnat ctccctaana      600
aatnctcctn naatttactn ncantnccat caancccaen tgaacnnnaa cccctgtttt      660
tanatccctt ctttcgaaaa ccnacccttt annncccaac ctttngggcc ccccnctnc      720
ccnaatgaag gncncccaat cnangaaacg nccntgaaaa ancnaggcna anannntccg      780
canatcctat cccttanttn ggggncctct ncccnngggc cc

```

<210> 30

<211> 787

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature



&lt;222&gt; (1)...(787)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 30

cgggccgctg	ctctggcaca	tgccctctga	atggcatcaa	aagtgatgga	ctgcccattg	60
ctagagaaga	ccttctctcc	tactgtcatt	atggagccct	gcagactgag	ggctccccct	120
gtctgcagga	tttgatgtct	gaagtcgtgg	agtgtggctt	ggagctcctc	atctacatna	180
gctggaagcc	ctggagggcc	tctctcgcca	gcctccccct	tctctccacg	ctctccangg	240
acaccagggg	ctccaggcag	cccattattc	ccagnangac	atggtgtttc	tccacgcgga	300
cccatggggc	ctgnaaggcc	agggctctct	ttgacaccat	ctctcccgtc	ctgcttgcca	360
ggccgtggga	tccactantt	ctanaacggn	cgccaccncg	gtgggagctc	cagcttttgt	420
tcccnttaat	gaaggttaat	tgcncgcttg	gcgtaatcat	nggtcanaac	tntttcctgt	480
gtgaaattgt	tnntcccttc	ncnattccnc	ncnacatacn	aaccgggaan	cataaagtgt	540
taaaagcctg	gggtngcctn	nngaataaac	tnaactcaat	taattgcgtt	ggctcatggc	600
ccgctttccn	ttcnggaaaa	ctgtcntccc	ctgenttnnt	gaatcgccca	ccccccnggg	660
aaaagcggtt	tgcnttttng	ggggntccct	ccncttcccc	cctcnctaan	ccctncgcct	720
cggtcgttnc	nggtngcggg	gaangggnat	nnnctccenc	naagggggng	agnnngntat	780
ccccaaa						787

&lt;210&gt; 31

&lt;211&gt; 799

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(799)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 31

tttttttttt	tttttttggc	gatgctactg	tttaattgca	ggaggtgggg	gtgtgtgtac	60
catgtaccag	ggctattaga	agcaagaagg	aaggaggagg	ggcagagcgc	cctgctgagc	120
aacaaaggac	tcttgcagcc	ttctctgtct	gtctcttggc	gcaggcacat	ggggaggcct	180
cccgaggggt	gggggcccacc	agtccagggg	tgggagcaet	acanggggtg	ggagtgggtg	240
gtggctggtn	cnaatggcct	gncacanatc	cctacgattc	ttgacacctg	gatttcacca	300
ggggaccttc	tgttttccca	nggnaacttc	ntnnatctcn	aaagaacaca	actgtttctt	360
cngcanttct	ggctgttcat	ggaaagcaca	ggtgtccnat	ttnggctggg	acttggtaca	420
tatggttccg	gcccacctct	cccntcnaa	aagtaattca	ccccccccc	ccntctnttg	480
cctgggcccct	taantaccca	caccggaact	canttantta	ttcatcttng	gntgggcttg	540
ntnatcnccn	cctgaangcg	ccaagttgaa	aggccacgcc	gtncenctc	cccatagnan	600
nttttnnent	canctaattg	ccccccnggc	aacnatccaa	tcccccccn	tgggggcccc	660
agcccanggc	ccccgncctg	ggnnncngn	cncgnantcc	ccagntctc	ccantcngnc	720
ccnnngcncc	cccgcacgca	gaacanaagg	ntngagccnc	cgcannnnnn	nggtncnnc	780
ctcgcccccc	ccnnecngng					799

&lt;210&gt; 32

&lt;211&gt; 789

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(789)

&lt;223&gt; n = A,T,C or G

```

<400> 32
tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt      60
tttttncnag ggcagggttta ttgacaacct cncgggacac aancaggctg gggacaggac      120
ggcaacaggc tcggcgggcg gcgcgggcgg ccctacctgc ggtaccaaat ntgcagcctc      180
cgctcccgct tgatnttccct ctgcagctgc aggatgcctt aaaacagggc ctgggccttn      240
ggtgggcacc ctgggatttn aatttccacg ggcacaatgc ggtcgcancc cctcaccacc      300
nattaggaat agtggtnnta cccnccnccg ttggcncact ccccnctggaa accacttntc      360
gcggtctcgg catctggtct taaaccttgc aaacnctggg gccctctttt tggttantnt      420
nccngccaca atcatnactc agactggcnc gggctggccc caaaaaancn ccccaaaacc      480
ggnccatgct ttnnccgggt tgctgcnatn tncatcacct cccgggcncn ncaggncac      540
ccaaaagtct ttgngcccn caaaaaanct ccggggggnc ccagtttcaa caaagtcate      600
ccccctggcc cccaaatcct ccccccgntt nctgggtttg ggaacccacg cctctnnctt      660
tggnnggcaa gntgntccc ccttcgggccc ccggtggggc ccnctcttaa ngaaacncc      720
ntcctnnnca ccatccccc nngnnacgnc tancaangna tccctttttt tanaaacggg      780
ccccccnccg

```

<210> 33

<211> 793

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(793)

<223> n = A,T,C or G

```

<400> 33
gacagaacat gttggatggt ggagcacctt tctatacgac ttacaggaca gcagatgggg      60
aattcatggc tgttggagca atanaacccc agttctacga gctgctgac aaaggacttg      120
gactaaagtc tgatgaacct cccaatcaga tgagcatgga tgattggcca gaaatgaana      180
agaagtttgc agatgtattt gcaaagaaga cgaaggcaga gtggtgtcaa atctttgacg      240
gcacagatgc ctgtgtgact ccggttctga cttttgagga ggttggtcat catgatcaca      300
acaangaacg gggctcgttt atcaccantg aggagcagga cgtgagcccc cgccttcgac      360
ctctgctgtt aaacacccca gccatccctt ctttcaaaa ggatccacta cttctagagc      420
ggnccgcccc gcggtggagc tccagctttt gttcccttta gtgagggtta attgcgcgct      480
tggcgtaatc atggctcatn ctgtttcctg tgtgaaattg ttatccgctc acaattccac      540
acaacatacy anccggaagc atnaaatttt aaagcctggn ggtngcctaa tgantgaact      600
nactcacatt aattggcttt gcgctcacty cccgctttcc agtccggaaa acctgtcctt      660
gccagctgcc nttaatgaat cnggccaccc cccggggaaa aggcngtttg cttnttgggg      720
cgcncttccc gctttctcgc ttcttgaant ccttccccc ggtctttcgg ctgcggcna      780
acggtatcna cct

```

<210> 34

<211> 756

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(756)

<223> n = A,T,C or G

```

<400> 34
gccgcgaccg gcatgtacga gcaactcaag ggcgagtggg accgtaaaag ccccaatctt      60
ancaagtgcg gggaanagct gggtcgactc aagctagtcc ttctggagct caacttcttg      120

```

```

ccaaccacag ggaccaagct gaccaaacag cagctaattc tggcccgtag catactggag      180
atcggggccc aatggagcat cctacgcaan gacatcccct ccttcgagcg ctacatggcc      240
cagctcaaat gctactactt tgattacaan gagcagctcc ccgagtcagc ctatatgcac      300
cagctcttgg gcctcaacct cctcttccctg ctgtcccaga accgggtggc tgantnccac      360
acgganttgg ancggtctgc tggccaanga catacanacc aatgtctaca tcnaccacca      420
gtgtcctgga gcaatactga tgganggcag ctaccncaa gntttccctg ccnagggtaa      480
catccccgcg cgagagctac acctttcttca ttgacatcct gctcgacact atcaggggatg      540
aaaatcgcn ggttgctcca gaaaggctnc aanaanatcc ttttcnctga aggcccccg      600
atnctagtg nctagaatcg gcccgccatc gcggtgganc ctccaacctt tcgtnccct      660
ttactgaggg ttnattgcg ccttggcgt tatcatggtc acncngttn cctgtgttga      720
aattntaac cccccaacat tccacgcna cattng      756

```

<210> 35

<211> 834

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(834)

<223> n = A,T,C or G

<400> 35

```

ggggatctct anactnacct gnatgcatgg ttgtcgggtg ggtcgctgtc gatgaanatg      60
aacaggatct tgcccttgaa gctctcggct gctgtnttta agttgctcag tctgccgtca      120
tagtcagaca cncctctggg caaaaaacan caggatntga gtcttgattt cactccaat      180
aatcttcngg gctgtctgct cggatgaactc gatgacnang ggcagctggg tgtgntgat      240
aaantccanc angttctcct tggtagacct ccttcaaaag ttgttcggc cttcatcaa      300
cttctnnaan angannancc canctttgtc gagctggnat ttgganaaca cgtcacrgt      360
ggaaactgat cccaaatggg atgtcatcca tcgctctgc tgctgcaaa aaacttgct      420
ggcncaaatc cgactcccn tccttgaaag aagccnatca cccccctc cctggactcc      480
nncaangact ctncgcctnc cccntccnng cagggttggg ggcannccgg gccntgcgc      540
ttcttcagcc agttcacnat ntctcatcag cctctgcca gctgtntat tccttggggg      600
ggaanccgtc tctcccttc tgaannaact ttgaccgtng gaatagccgc gcntcncnt      660
acntnctggg ccgggttcaa antccctcn ttgncnntcn cctcgggcca ttctggattt      720
nccnaacttt ttccttcccc cnccccncgg ngtttggntt tttcatnggg ccccaactct      780
gctnttggcc antcccttg gggcntntan cnccccctnt ggtccctnng ggcc      834

```

<210> 36

<211> 814

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(814)

<223> n = A,T,C or G

<400> 36

```

cggncgcttt ccngccgcgc cccgtttcca tgacnaaggg tcccttcang ttaaatacnn      60
cctagnaaac attaatgggt tgctctacta atacatcata cnaaccagta agcctgccca      120
naacgccaac tcaggccatt cctaccaaag gaagaaaggg tggctctctc acccctgta      180
ggaaaggcct gccttgtaag acaccacaat ncggctgaat ctnaagtctt gtgtttact      240
aatggaaaaa aaaaaataac aanaggtttt gttctcatgg ctgcccaccg cagcctggca      300
ctaaaacanc ccagcgctca cttctgcttg ganaaatatt ctttgctctt ttggacatca      360

```

```

ggcttgatgg tactactgcc acntttccac ccagctgggc ncccttcccc catntttgtc 420
antganctgg aaggcctgaa ncttagtctc caaaagtctc ngcccacaag accggccacc 480
agggggangtc ntttncagtg gatctgccaa anantaccn tatcatcnnt gaataaaaaag 540
gcccttgaac ganatgcttc cancanctt taagaccat aatcctngaa ccatgggtgcc 600
cttccegtct gatccnaaag gaatgttctt gggteccant cctctctttg ttntctacgt 660
tgtnttgga cctngctngn atnacccaan tganatcccc ngaagcacc tncacctggc 720
atttganttt cntaaattct ctgccctacn nctgaaagca cnattccctn ggcncnnaan 780
ggngaactca agaaggtctn ngaaaaacca cncn 840

```

&lt;210&gt; 37

&lt;211&gt; 760

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(760)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 37

```

gcctgctgct cttccctaaa gttgttcttg ttgccataac aaccaccata ggtaaacggy 60
gcgcagtgt cgctgaaggg gttgtagtac cagcgcggga tgctctcctt gcagagctct 120
gtgtctggca ggtccacgca atgccctttg tcaactggga aatggatgcy ctggagctcg 180
tcnaaaccac tcgtgtattt ttcacangca gcctcctccg aagcctccgg gcagttgggy 240
gtgtcgtcac actccactaa actgtcgatn cancacccca ttgctgcagc ggaactgggt 300
gggctgacag gtgccagaac acactggatn ggctcttcca tggaaaggcc tgggggaaat 360
cncctnanc caaactgcct ctcaaaggcc accttgcaca ccccgacagg ctagaaatgc 420
actcttcttc ccaaaggtag ttgttcttgt tgcccaagca ncctccanca aaccaaanc 480
ttgcaaaatc tgctccgtgg gggcatnnn taccanggtt ggggaaanaa acccgcgngn 540
gancncctt gtttgaatgc naaggnaata atcctcctgt cttgcttggg tggaaanagca 600
caattgaact gttaaacttg gggcngttc cncnnggggt gtctgaaact aatcacctgc 660
actggaaaaa ggtangtgcc ttccttgaat tcccaaannt cccctngntt tgggtntttt 720
ctcctctncc ctaaaaatcg tntccccccc centanggcy 760

```

&lt;210&gt; 38

&lt;211&gt; 724

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(724)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 38

```

tttttttttt tttttttttt tttttttttt tttttaaaaa cccctccat tgaatgaaaa 60
cttccnaaat tgtccaaccc cctcnnccaa atnncattt ccgggggggg gttccaaacc 120
caaatattt ttgganttta aattaaatnt tnatnngggg aanaanccaa atgtnaagaa 180
aatttaaccc attatnaact taaatnctn gaaaccntg gnttccaaaa atttttaacc 240
cttaaattccc tccgaatttg ntaanggaaa accaaattcn cctaaggctn ttgaaagggt 300
ngatttaaac ccccttnant tnttttacc cnnngctnaa ntatttngnt tccggtgttt 360
tcctnttaan cntnggtaac tcccgntaat gaannncctt aanccaatta aaccgaattt 420
tttttgaaat ggaaattccn ngggaattna ccgggggttt tccctnttgg gggccatncc 480
cccnctttcg ggggttgggn ntagggtgaa ttttttnang nccccaaaaa ncccccaana 540
aaaaaactcc caagnnttaa ttngaantnc ccccttccca ggccttttgg gaaaggnggy 600

```

```

tttntggggg ccnggggantt cnttcccccn ttncncccc cccccnggt aaanggttat 660
ngnnttttgt ttttgggccc cttnanggac cttccggatn gaaattaaat cccccggngc 720
gccg 724

```

```

<210> 39
<211> 751
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(751)
<223> n = A,T,C or G

```

```

<400> 39
tttttttttt tttttctttg ctcacattta atttttattt tgattttttt taatgtgtga 60
caacacaata tttatttcat ttgtttcttt tatttcattt tatttgtttg ctgctgctgt 120
tttatttatt tttactgaaa gtgagaggga acttttgttg ccttttttcc tttttctgta 180
ggccgcctta agctttctaa atttggaaac tctaagcaag ctgaanggaa aaggggggtt 240
cgcaaaatca ctccggggaa nggaaagggt gctttgttaa tcatgcccta tgggtgggtga 300
ttaactgctt gtacaattac ntttcacttt taattaattg tgctnaangc ttaattana 360
cttgggggtt ccctccccc accaacccon ctgacaaaaa gtgcngccc tcaaatnatg 420
tcccggcnnt cnttgaaaca cacngcngaa ngttctcatt ntcccnccnc caggtnaaaa 480
tgaagggtta ccatntttaa cncacctcc acntggcnnn gcctgaatcc tcnaaaannc 540
ccctcaannc aattnctnng ccccggtcnc gcntnngtc cncccgggct ccgggaantn 600
cacccccnga annncntnnc naacnaaatt ccgaaaaat tcccnntcnc tcaattcccc 660
cnnagactnt cctcnnncan cnaaatttc ttttnntcac gaacncgnc cnnaaatgtn 720
nnnncnctc cncntngtcn naatcnccan c 751

```

```

<210> 40
<211> 753
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(753)
<223> n = A,T,C or G

```

```

<400> 40
gtggtatttt ctgtaagatc aggtgttcc ccttcgtagg tttagaggaa acaccctcat 60
agatgaaaac ccccccgaga cagcagcact gcaactgcc aagcagccgg gtaggagggg 120
cgccctatgc acagctgggc ccttgagaca gcagggtctc gatgtcaggc tcgatgtcaa 180
tggtctggaa gcggcggtg tacctgcgta ggggcacacc gtcaggggccc accaggaact 240
tctcaaagtt ccaggcaacn tcgttgcgac acaccggaga ccagggtatn agcttgggggt 300
cggtcataaa cgcgggtggc tcgtcgtctg gagctggcag ggcctcccgc aggaaggcna 360
ataaaagggt cgcccccgca ccgttcantc cgcacttctc naanaccatg angttgggct 420
cnaaccacc accannccgg acttctctga nggaattccc aaatctcttc gntcttgggc 480
ttctnctgat gccctantcg gttgcccn gn atgccaanca nccccaancc ccgggggtcct 540
aaanaccen cctcctcntt tcatctgggt tnttntcccc ggaccttggt tcctctcaag 600
gnaaccata tctcnaccan tactcaccnt nccccccnt gnnaccanc cttctanngn 660
ttccncccg ncctctggcc cntcaaan gcttnacna cctgggtctg ccttcccccc 720
tnccctatct gnaccnncn ttgtctcan tnt 753

```

```

<210> 41

```

<211> 341  
 <212> DNA  
 <213> Homo sapien

<400> 41  
 actatatcca tcacaacaga catgcttcat cccatagact tcttgacata gcttcaaatg 60  
 agtgaaccca tccttgattt atatacatat atgttctcag tattttggga gcctttccac 120  
 ttctttaaac cttgttcatt atgaacactg aaaataggaa ttgtgaaga gttaaaaagt 180  
 tatagcttgt ttacgtagta agtttttgaa gtctacattc aatccagaca cttagttgag 240  
 tgttaaactg tgatttttaa aaaatatcat ttgagaatat tctttcagag gtattttcat 300  
 ttttactttt tgattaattg tgttttatat attagggtag t 341

<210> 42  
 <211> 101  
 <212> DNA  
 <213> Homo sapien

<400> 42  
 atttactgaa tttagtctg tgctcttctt tattttagtgt tgtatcataa atactttgat 60  
 gtttcaaaca ttctaaataa ataattttca gtggcttcat a 101

<210> 43  
 <211> 305  
 <212> DNA  
 <213> Homo sapien

<400> 43  
 acatctttgt tacagtctaa gatgtgttct taaatcacca ttccttctctg gtcttcaccc 60  
 tccaggggtgg tctcacactg taattagagc tattgaggag tctttacagc aaattaagat 120  
 tcagatgctt tgctaagctt agagttctag agttatgttt cagaaaagtct aagaaaccca 180  
 cctcttgaga ggtcagtaaa gaggacttaa tatttcatat ctacaaaatg accacaggat 240  
 tggatacaga acgagagtta tcctggataa ctacagagctg agtacctgcc cgggggccgc 300  
 tcgaa 305

<210> 44  
 <211> 852  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (852)  
 <223> n = A, T, C or G

<400> 44  
 acataaatat cagagaaaag tagtctttga aatattttacg tccaggaggt ctttgtttct 60  
 gattatttgg tgtgtgtttt ggtttgtgtc caaagtattg gcagcttcag ttttcatttt 120  
 ctctccatcc tcgggcattc ttcccaaatt tataataccag tcttcgtcca tccacacgct 180  
 ccagaatttc tctttttag tagtatctca tagctcggt gagcttttca taggtcatgc 240  
 tgctgttgtt cttcttttta ccccatagct gagccactgc ctctgatttc aagaacctga 300  
 agacgccctc agatcggtct tcccatttta ttaatcctgg gttctgtgtc gggttcaaga 360  
 ggatgtcgcg gatgaattcc cataagttag tccctctcgg gttgtgtctt ttggtgtggc 420  
 acttggcagg ggggtcttgc tcttttttca tatcagggtga ctctgcaaca ggaagggtgac 480  
 tgggtgtgtc catggagatc tgagcccgcc agaaagtatt gctgtccaac aaatctactg 540  
 tgctaccata gttggtgtca tataaatagt tctngtcttt ccagggtgtc atgatggaag 600

```

gctcagtttg ttcagtccttg acaatgacat tgtgtgtgga ctggaacagg tcactactgc      660
actggccggt ccacttcaga tgcctgcaagt tgctgtagag gagntgcccc gccgtccctg      720
ccgccgggt gaactcctgc aaactcatgc tgcaaagggt ctgcgcgttg atgtcgaaact      780
cntggaaagg gatacaattg gcatccagct ggttggtgtc caggaggtga tggagccact      840
ccacacactg gt                                     852

```

```

<210> 45
<211> 234
<212> DNA
<213> Homo sapien

```

```

<400> 45
acaacagacc cttgctcgct aacgacctca tgcctcatca gttggacgaa tccgtgtccg      60
agtctgacac catccggagc atcagcattg ctctgcagtg ccctaccgcg gggaactcct      120
gcctcgtttc tggctgggggt ctgctggcga acggcagaat gcctaccgtg ctgcagtgcg      180
tgaacgtgtc ggttggtgtc gaggagggtc gcagtaagct ctatgacccc ctgt          234

```

```

<210> 46
<211> 590
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (590)
<223> n = A,T,C or G

```

```

<400> 46
actttttatt taaatgttta taaggcagat ctatgagaat gatagaaaac atgggtgtgta      60
atttgatagc aatatttttg agattacaga gttttagtaa ttaccaatta cacagttaaa      120
aagaagataa tatattccaa gcanatacaa aatatcctaat gaaagatcaa ggcaggaaaaa      180
tgantataac taattgacaa tggaaaatca attttaatgt gaattgcaca ttatccttta      240
aaagctttca aaanaanaaa ttattgcagt ctanttaatt caaacagtggt taaatgggtat      300
caggataaan aactgaaggg canaaaagaat taattttcac ttcatgtaac ncacccanat      360
ttacaatggc ttaaatgcan gaaaaaagca gtggaagtag ggaagtantc aaggtctttc      420
tggctcttaa tctgccttac tctttgggtg tggctttgat cctctggaga cagctgccag      480
ggctcctgtt atatccacaa tcccgcagc aagatgaagg gatgaaaaag gacacatgct      540
gccttccttt gaggagactt catctcactg gccaacactc agtcacatgt          590

```

```

<210> 47
<211> 774
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (774)
<223> n = A,T,C or G

```

```

<400> 47
acaagggggc ataatgaagg agtgggggana gattttaaag aaggaaaaaa aacgaggccc      60
tgaacagaat tttcctgnac aacgggggctt caaaataatt ttcttgggga ggttcaagac      120
gcttcactgc ttgaaactta aatggatgtg ggacanaatt ttctgtaatg accctgaggg      180
cattacagac gggactcttg gaggaaggat aaacagaaag gggacaaaag ctaatcccaa      240
aacatcaaag aaaggaaggt ggcgtcatac ctccagcct acacagtctt ccagggtctt      300

```

```

cctcatccct ggaggacgac agtggaggaa caactgacca tgtccccagg ctctctgtgtg      360
ctggctcctg gtcttcagcc cccagctctg gaagcccacc ctctgctgat cctgcgtggc      420
ccacactcct tgaacacaca tccccagggt atattcctgg acatggctga acctcctatt      480
cctacttccg agatgccttg ctccctgcag cctgtcaaaa tcccactcac cctccaaacc      540
acggcatggg aagcctttct gacttgcctg attactccag catcttggaa caatccctga      600
ttccccactc cttagaggca agataggggt gttaagagta gggctggacc acttgaggcc      660
aggctgctgg cttcaaattn tggctcattt acgagctatg ggaccttggg caagtnatct      720
tcacttctat gggcntcatt ttgttctacc tgcaaaatgg gggataataa tagt          774

```

<210> 48

<211> 124

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(124)

<223> n = A,T,C or G

<400> 48

```

canaaattga aattttataa aaaggcattt ttctcttata tccataaaat gatataattt      60
ttgcaantat anaaatgtgt cataaattat aatgttcctt aattacagct caacgcaact      120
tggt                                              124

```

<210> 49

<211> 147

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(147)

<223> n = A,T,C or G

<400> 49

```

gccgatgcta ctattttatt gcaggagggt ggggtgtttt tattattctc tcaacagctt      60
tgtggctaca ggtggtgtct gactgcatna aaaanttttt tacgggtgat tgcaaaaatt      120
ttagggcacc catatcccaa gcantgt                                              147

```

<210> 50

<211> 107

<212> DNA

<213> Homo sapien

<400> 50

```

acattaaatt aataaaaagga ctgttgggggt tctgctaaaa cacatggctt gatatatattgc      60
atggtttgag gttaggagga gttaggcata tgttttggga gaggggt                      107

```

<210> 51

<211> 204

<212> DNA

<213> Homo sapien

<400> 51

```

gtcctaggaa gtctagggga cacacgactc tggggtcacg gggccgacac acttgcacgg      60

```



```

cggggaaggaa aggcagagaa gtgacaccgt caggggggaaa tgacagaaaag gaaaatcaag 120
gccttgcaag gtcagaaaagg ggatccaggg ctccaccac agccctgccc cacttgccca 180
cctccctttt gggaccagca atgt 204

```

```

<210> 52
<211> 491
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(491)
<223> n = A,T,C or G

```

```

<400> 52
acaaagataa catttatctt ataacaataa ttgatagtt ttaaagggtta gtattgtgta 60
gggtattttc caaaagacta aagagataac tcaggtaaaa agttagaaat gtataaaaca 120
ccatcagaca ggttttttaa aaacaacata ttacaaaatt agacaatcat ccttaaaaaa 180
aaaacttctt gtatcaattt cttttgttca aaatgactga cttaatattt tttaaatatt 240
tcanaaacac ttctcaaaa attttcaana tggtagcttt canatgtnc ctcagtccca 300
atgttgctca gataaataaa tctcgtgaga acttaccacc caccacaagc tttctggggc 360
atgcaacagt gtcttttctt tnccttttct ttttttttt ttacaggcac agaaaactcat 420
caattttatt tggataacaa agggctctcca aatttatattg aaaaataaat ccaagttaat 480
atcactcttg t 491

```

```

<210> 53
<211> 484
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(484)
<223> n = A,T,C or G

```

```

<400> 53
acataattta gcagggctaa ttaccataag atgctattta ttaanaggtn tatgatctga 60
gtattaaacag ttgctgaagt ttggattttt tatgcagcat tttctttttt ctttgataac 120
actacagaac ccttaaggac actgaaaatt agtaagtataa gttcagaaac attagctgct 180
caatcaaact tctacataac actatagtaa ttaaaacgtt aaaaaaaagt gttgaaatct 240
gcactagat anaccgctcc tgtcaggata anactgcttt ggaacagaaa gggaaaaaac 300
agctttgant ttctttgtgc tgatangagg aaaggctgaa ttacctgtt gcctctccct 360
aatgattggc aggtcnggta aatnccaaaa catattccaa ctcaacactt cttttccnng 420
tancttgant ctgtgtattc caggancagg cggtatggaat gggccagccc ncggatgttc 480
cant 484

```

```

<210> 54
<211> 151
<212> DNA
<213> Homo sapien

```

```

<400> 54
actaaacctc gtgcttgatg actccatata gaaaacgggtg ccactccctga acacggctgg 60
ccactgggta tactgctgac aaccgcaaca acaaaaaacac aaatccttgg cactggctag 120
tctatgtcct ctcaagtgcc tttttgttg t 151

```

<210> 55  
 <211> 91  
 <212> DNA  
 <213> Homo sapien

<400> 55  
 acctggcttg tctccgggtg gttcccggcg cccccacgg tccccagaac ggacactttc 60  
 gccctccagt ggatactcga gccaaagtgg t 91

<210> 56  
 <211> 133  
 <212> DNA  
 <213> Homo sapien

<400> 56  
 ggcggatgtg cgttggttat atacaaatat gtcattttat gtaagggact tgagtatact 60  
 tggatttttg gtattctgtg gttgggggga cgggtccagga accaatatcc catggatacc 120  
 aagggacaac tgt 133

<210> 57  
 <211> 147  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(147)  
 <223> n = A,T,C or G

<400> 57  
 actctggaga acctgagccg ctgctccgcc tctgggatga ggtgatgcan gcngtggcgc 60  
 gactggggagc tgagcccttc cctttgcgcc tgctcagag gattgttgcc gacntgcana 120  
 tctcantggg ctggatncat gcagggt 147

<210> 58  
 <211> 198  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(198)  
 <223> n = A,T,C or G

<400> 58  
 acagggatat aggtttnaag ttattgtnat tgtaaaatc attgaatttt ctgtatactc 60  
 tgattacata catttatcct ttaaaaaaga tgtaaatctt aatttttatg ccacttatta 120  
 atttaccat gagttacctt gtaaatgaga agtcatgata gcactgaatt ttaactagtt 180  
 ttgacttcta agtttggt 198

<210> 59  
 <211> 330  
 <212> DNA  
 <213> Homo sapien

<400> 59  
acaacaaatg ggttgtgagg aagtctttatc agcaaaaactg gtgatggcta ctgaaaagat 60  
ccattgaaaa ttatcattaa tgattttaaa tgacaagtta tcaaaaactc actcaatttt 120  
cacctgtgct agcttgcctaa aatgggagtt aactctagag caaatatagt atcttctgaa 180  
tacagtcaat aaatgacaaa gccagggcct acaggtggtt tccagacttt ccagaccag 240  
cagaaggaat ctattttatc acatggatct ccgtctgtgc tcaaaaatacc taatgatatt 300  
tttcgtcttt attggacttc tttgaagagt 330

<210> 60  
<211> 175  
<212> DNA  
<213> Homo sapien

<400> 60  
accgtgggtg ccttctacat tcctgacggc tccttcacca acatctggtt ctacttcggc 60  
gtcgtgggct ccttcctctt catctcatc cagctgggtc tgctcatcga ctttgcgcac 120  
tcctggaacc agcggtaggt gggcaaggcc gaggagtgcg attcccgtgc ctggt 175

<210> 61  
<211> 154  
<212> DNA  
<213> Homo sapien

<400> 61  
accccacttt tcctcctgtg agcagtctgg acttctcact gctacatgat gagggtgagt 60  
ggttgttgcct cttcaacagt atctctccct ttccggatct gctgagccgg acagcagtc 120  
tggactgcac agccccgggg ctccacattg ctgt 154

<210> 62  
<211> 30  
<212> DNA  
<213> Homo sapien

<400> 62  
cgctcgagcc ctatagtgag tcgtattaga 30

<210> 63  
<211> 89  
<212> DNA  
<213> Homo sapien

<400> 63  
acaagtcatt tcagcacctt ttgctcttca aaactgacca tcttttatat ttaatgcttc 60  
ctgtatgaat aaaaatgggt atgtcaagt 89

<210> 64  
<211> 97  
<212> DNA  
<213> Homo sapien

<400> 64  
accggagtaa ctgagtcggg acgctgaatc tgaatccacc aataaataaa ggttctgcag 60  
aatcagtcga tccaggattg gtccttggat ctggggg 97

<210> 65  
 <211> 377  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (377)  
 <223> n = A,T,C or G

<400> 65  
 acaacaanaa ntcccttctt tagggcactg atggaaacct ggaacccctt ttgatggca 60  
 gcatggcgtc ctaggccttg acacagcggc tggggtttgg gctntcccaa accgcacacc 120  
 ccaaccctgg tctaccaca nttctggcta tgggctgtct ctgccactga acatcagggg 180  
 tcggtcataa natgaaatcc caanggggac agaggtcagt agaggaagct caatgagaaa 240  
 ggtgctgttt gctcagccag aaaacagctg cctggcattc gccgctgaac tatgaacccg 300  
 tgggggtgaa ctacccccan gaggaatcat gcctgggcga tgcaanggtg ccaacaggag 360  
 gggcgggagg agcatgt 377

<210> 66  
 <211> 305  
 <212> DNA  
 <213> Homo sapien

<400> 66  
 acgcctttcc ctacagaattc agggaagaga ctgtcgcttg ccttctctcg ttgttgctg 60  
 agaaccctg tgcccccttc caccatatcc acctctgctc catctttgaa ctcaaacacg 120  
 aggaactaac tgcacctgg tcctctcccc agtccccagt tcacctcca tccctcacct 180  
 tcctccactc taagggatat caacactgcc cagcacaggg gccctgaatt tatgtggttt 240  
 ttatatattt ttaataaaga tgcactttat gtcatttttt aataaagtct gaagaattac 300  
 tgttt 305

<210> 67  
 <211> 385  
 <212> DNA  
 <213> Homo sapien

<400> 67  
 actacacaca ctccacttgc ctttgtgaga cactttgtcc cagcacttta ggaatgctga 60  
 ggtcggacca gccacatctc atgtgcaaga ttgcccgca gacatcaggt ctgagagttc 120  
 cccttttaaa aaaggggact tgcttaaaaa agaagtctag ccacgattgt gttagagcagc 180  
 tgtgtgtgctc tggagattca cttttgagag agttctcctc tgagacctga tctttagagg 240  
 ctgggcagtc ttgcacatga gatggggctg gtctgatctc agcactcctt agtctgcttg 300  
 cctctcccag ggccccagcc tggccacacc tgcttacagg gcactctcag atgcccatac 360  
 catagtttct gtgctagtgg accgt 385

<210> 68  
 <211> 73  
 <212> DNA  
 <213> Homo sapien

<400> 68  
 acttaaccag atatattttt accccagatg gggatattct ttgtaaaaaa tgaaaataaa 60  
 gtttttttaa tgg 73

<210> 69  
 <211> 536  
 <212> DNA  
 <213> Homo sapien  
  
 <220>  
 <221> misc\_feature  
 <222> (1)... (536)  
 <223> n = A,T,C or G

<400> 69  
 actagtccag tgtggtggaa ttccattgtg ttgggggctc tcaccctcct ctccctgcagc 60  
 tccagctttg tgctctgcct ctgaggagac catggcccag catctgagta ccctgctgct 120  
 cctgctggcc accctagctg tggccctggc ctggagcccc aaggaggagg ataggataat 180  
 cccgggtggc atctataacg cagacctcaa tgatgagtgg gtacagcgtg cccttcactt 240  
 cgccatcagc gagtataaca aggccaccaa agatgactac tacagacgtc cgctgcgggt 300  
 actaagagcc aggcaacaga ccgttggggg ggtgaattac ttcttcgcag tagagggtgg 360  
 ccgaaccata tgtaccaagt cccagcccaa ctggacacc tgtgccttcc atgaacagcc 420  
 agaactgcag aagaaacagt tgtgctcttt cgagatctac gaagtccct ggggagaaca 480  
 gaangtcctt gggtgaaatc cagggtgtcaa gaaatcctan ggatctgttg ccagggc 536

<210> 70  
 <211> 477  
 <212> DNA  
 <213> Homo sapien

<400> 70  
 atgaccctta acaggggccc tctcagccct cctaatgacc tccggcctag ccatgtgatt 60  
 tcacttccac tccataacgc tccctcactt aggcctacta accaaccacac taaccatata 120  
 ccaatgatgg cgcgatgtaa cagagaaaag cacataccaa ggccaccaca caccacctgt 180  
 ccaaaaaagg cttcgatacg ggataatcct atttattacc tcagaagttt ttttcttcgc 240  
 agggattttt ctgagccttt taccactcca gcctagcccc taccceccaa ctaggaggggc 300  
 actggccccc aacaggcctc accccgctaa atcccctaga agtcccactc ctaaacacat 360  
 ccgtattact cgcattcagg gtatcaatca cctgagctca ccatagtcta atagaaaaca 420  
 accgaaacca aattattcaa agcactgctt attacaattt tactgggtct ctatttt 477

<210> 71  
 <211> 533  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)... (533)  
 <223> n = A,T,C or G

<400> 71  
 agagctatag gtacagtgtg atctcagctt tgcaaacaca ttttctacat agatagtact 60  
 aggtattaat agatatgtaa agaagaaat cacaccatta ataatggtaa gattggttta 120  
 tgtgatttta gtggtatttt tggcaccctt atatatgttt tccaaacttt cagcagtgat 180  
 attatttcca taacttaaaa agtgagtgtt aaaaagaaaa tctccagcaa gcatctcatt 240  
 taaataaagg tttgtcatct ttaaaaaatac agcaatatgt gactttttaa aaaagctgtc 300  
 aaatagggtg gaccctacta ataattatta gaaatacatt taaaaacatc gagtacctca 360  
 agtcagtttg ccttgaaaaa tatcaaatat aactcttaga gaaatgtaca taaaagaatg 420  
 cttcgtaatt ttggagtang aggttccttc ctcaattttg tattttttaa aagtacatgg 480  
 taaaaaaaaa aattcacacac agtatataag gctgtaaaat gaagaatttc gcc 533

<210> 72  
 <211> 511  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(511)  
 <223> n = A,T,C or G

<400> 72  
 tattacggaa aaacacacca cataattcaa ctancaaaga anactgcttc agggcggtga 60  
 aaatgaaagg cttccaggca gttatctgat taaagaacac taaaagaggg acaaggctaa 120  
 aagccgcagg atgtctacac tatancaggc gctatttggg ttggctggag gagctgtgga 180  
 aaacatggan agatttggtgc tgganacgc cgtggctatt cctcattgtt attacanagt 240  
 gaggttctct gtgtgcccac tggtttgaaa accgttctnc aataatgata gaatagtaca 300  
 cacatgagaa ctgaaatggc ccaaaccag aaagaaagcc caactagatc ctcagaanac 360  
 gcttctaggg acaataaccg atgaagaaaa gatggcctcc ttgtgcccc gtctgttatg 420  
 atttctctcc attgcagcna naaaccggtt cttctaagca aancnagggt atgatggcna 480  
 aaatacaccc cctcttgaag naccnggagg a 511

<210> 73  
 <211> 499  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(499)  
 <223> n = A,T,C or G

<400> 73  
 cagtgccagc actggtgccg gtaccagtag caataacagt gccagtgccg gtgccagcac 60  
 cagtggtagc ttcatgtctg gtgccagcct gaccgccact ctcacatttg ggctcttcgc 120  
 tggccttggt ggagctgggt ccagcaccag tggcagctct ggtgcctgtg gtttctccta 180  
 caagttagat ttttagatatt gttaatcctg ccagtctttc tcttcaagcc aggggtgcatc 240  
 ctcagaaacc tactcaacac agcactctag gcagccacta tcaatcaatt gaagttgaca 300  
 ctctgcatta aatctatttg ccatttctga aaaaaaaaaa aaaaaaaggg cggccgctcg 360  
 antctagagg gcccgtttaa acccgctgat cagcctcgac tgtgccttct anttgccagc 420  
 catctgttgt ttgccccctc ccgntgcct tccttgaccc tggaaagtgc cactcccact 480  
 gtcctttctc aantaaaaa 499

<210> 74  
 <211> 537  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(537)  
 <223> n = A,T,C or G

<400> 74  
 tttcatagga gaacacactg aggagatact tgaagaattt ggattcagcc gcgaagagat 60

```

tctatcagctt aactcagata aaatcattga aagtaataag gtaaaagcta gtctctaact 120
tccaggccca cggctcaagt gaatttgaat actgcattta cagtgtagag taacacataa 180
cattgtatgc atggaaacat ggaggaaacag tattacagtg tcttaccact ctaatcaaga 240
aaagaattac agactctgat tctacagtga tgattgaatt ctaaaaatgg taatcattag 300
ggcttttgat ttataaact ttgggtactt atactaaatt atggtagtta tactgccttc 360
cagtttgctt gatataattg ttgatattaa gattcttgac ttatatattg aatgggttct 420
actgaaaaan gaatgatata ttcttgaaga catcgatata catttattta cactcttgat 480
tctacaatgt agaaaatgaa ggaaatgccc caaattgtat ggtgataaaa gtcccgct 537

```

<210> 75

<211> 467

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(467)

<223> n = A,T,C or G

<400> 75

```

caaanacaat tgttcaaaa atgcaaatga tacactactg ctgcagctca caaacacctc 60
tgcatattac acgtacctcc tcttgcctcc caagtagtgt ggtctatttt gccatcatca 120
cctgctgtct gcttagaaga acggctttct gctgcaangg agagaaatca taacagacgg 180
tggcacaagg aggccatctt ttcctcatcg gttattgtcc ctagaagcgt cttctgagga 240
tctagttggg ctttctttct ggggttgggc catttcantt ctcatgtgtg tactattcta 300
tcattattgt ataacggttt tcaaaccnct gggcacncag agaacctcac tctgtaataa 360
caatgaggaa tagccacggt gatctccagc accaaatctc tccatgttnt tccagagctc 420
ctccagccaa cccaaatagc cgctgctatn gtgtagaaca tccctgn 467

```

<210> 76

<211> 400

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(400)

<223> n = A,T,C or G

<400> 76

```

aagctgacag cattcggggc gagatgtctc gctccgtggc cttagctgtg ctgcgctac 60
tctctctttc tggcctggag gctatccagc gtactccaaa gattcagggt tactcacgtc 120
atccagcaga gaatggaaa tcaaatttcc tgaattgcta tgtgtctggg ttcatccat 180
ccgacattga agttgactta ctgagaagt gagagagaat tgaaaaagtg gagcattcag 240
acttgctttt cagcaaggac tggctttct atctcttgta ctacactgaa ttcaccccca 300
ctgaaaaaga tgagtatgcc tgccgtgtga accatgtgac tttgtcacag cccaagatng 360
ttnagtgga tcganacatg taagcagcan catgggaggt 400

```

<210> 77

<211> 248

<212> DNA

<213> Homo sapien

<400> 77

```

ctggagtgcc ttggtgtttc aagcccctgc aggaagcaga atgcaccttc tgaggcacct 60

```

```

ccagctgccc cggcggggga tgcgaggctc ggagcaccct tgcccggctg tgattgctgc      120
caggcactgt tcatctcagc tttctgtccc ctttgcctcc ggcaagcgct tctgtgaaa      180
gttcatactc ggagcctgat gtcttaacga ataaaggctc catgctccac ccgaaaaaaa      240
aaaaaaaaa                                     248

```

```

<210> 78
<211> 201
<212> DNA
<213> Homo sapien

```

```

<400> 78
actagtccag tgtggtggaa ttccattgtg ttgggcccac cacaatggct acctttaaca      60
tcacccagac ccgcgccctgc ccgtgcccca cgctgctgct aacgacagta tgatgcttac      120
tctgctactc ggaaactatt tttatgtaat taatgtatgc tttctgttt ataatgcct      180
gatttaaaaa aaaaaaaaaa a                                     201

```

```

<210> 79
<211> 552
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (552)
<223> n = A,T,C or G

```

```

<400> 79
tccttttgtt aggtttttga gacaacccta gacctaaact gtgtcacaga cttctgaatg      60
tttaggcagt gctagtaatt tcctcgtaat gattctgtta ttactttcct attctttatt      120
cctctttcct ctgaagatta atgaagtga aaattgaggt ggataaatac aaaaaggtag      180
tgtgatagta taagtatcta agtcagatg aaagtgtgtt atatatatcc attcaaaatt      240
atgcaagtta gtaattactc aggggttaact aaattacttt aatagtctgt tgaacctact      300
ctgttccttg gctagaaaaa attataaaca ggactttgtt agtttgggaa gccaaattga      360
taatatctta tgttctaaaa gttgggctat acataaanta tnaagaaata tggaatttta      420
ttcccaggaa tatggggttc atttatgaat antaccggg anagaagttt tgantnaaac      480
cngtttttgt taatacgtta atagtctctn aatnaacaag gcntgactta ttccaaaaa      540
aaaaaaaaa aa                                             552

```

```

<210> 80
<211> 476
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (476)
<223> n = A,T,C or G

```

```

<400> 80
acagggattt gagatgctaa ggccccagag atcgtttgat ccaaccctct tattttcaga      60
ggggaaaaatg gggcctagaa gttacagagc atctagctgg tgcgctggca ccctggcct      120
cacacagact cccgagtagc tgggactaca ggcacacagt cactgaagca ggccctgttt      180
gcaattcacg ttgccacctc caacttaaac attcttcata tgtgatgtcc ttagtcaact      240
aggttaacct ttcccaccca gaaaaggcaa cttagataaa atcttagagt actttcatatc      300
tcttctaagt cctcttccag cctcactttg agtcctcctt ggggggttgat aggaantntc      360

```



tcttggcttt ctcaataaaa tctctatcca tctcatgttt aatttggtag gcntaaaaat 420  
gctgaaaaaa ttaaaatgtt ctggtttcnc tttaaaaaaa aaaaaaaaaa aaaaaa 476

<210> 81  
<211> 232  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(232)  
<223> n = A,T,C or G

<400> 81  
tttttttttg tatgcntcn ctgtggngtt attgttgetg ccaccttga ggagcccagt 60  
ttctttctga tctttctttt ctgggggac ttcttggctc tgcccctcca tttccagcct 120  
ctcatcccca tcttgcactt ttgctagggt tggaggcgct ttcttggtag cccctcagag 180  
actcagtcag cggaataag tcttaggggt ggggggtgtg gcaagccggc ct 232

<210> 82  
<211> 383  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(383)  
<223> n = A,T,C or G

<400> 82  
aggcgggagc agaagctaaa gccaaagccc aagaagagtg gcagtgccag cactgggtgcc 60  
agtaccagta ccaataacat gccagtgccca gtgccagcac cagtgggtggc ttcagtgtctg 120  
gtgccagcct gaccgccact ctcacatttg ggctcttcgc tggccttggt ggagctgggtg 180  
ccagcaccag tggcagctct ggtgcctgtg gttcttccta caagtgaagt tttagatatt 240  
gttaatcctg ccagtctttc tcttcaagcc aggggtgcac ctcagaaacc tactcaacac 300  
agcactctng gcagccacta tcaatcaatt gaagttgaca ctctgcatta aatctatttg 360  
ccatttcaaa aaaaaaaaaa aaa 383

<210> 83  
<211> 494  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(494)  
<223> n = A,T,C or G

<400> 83  
accgaatttg gaccgtggc ttataagcga tcatgtcctc cagtattacc tcaacgagca 60  
gggagatcga gtctatacgc tgaagaaatt tgaccgatg ggacaacaga cctgctcagc 120  
ccatcctgct cggttctccc cagatgacaa atactctcga caccgaatca ccatcaagaa 180  
agcgttcaag gtgctcatga ccagcaacc gcgcctgtc ctctgagggt cctttaaactg 240  
atgtcttttc tgccacctgt taccctcgg agactccgta accaaactct tcggactgtg 300  
agccctgatg cctttttgcc agccatactc ttggcctcc agtctctcgt ggcgattgat 360

```

tatgcttggtg tgaggcaatc atggtggcat caccatnaa gggaacacat ttganttttt 420
tttncatcat tttaaattac naccagaata ntccagaata aatgaattga aaaactctta 480
aaaaaaaaaa aaaa 494

```

```

<210> 84
<211> 380
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(380)
<223> n = A,T,C or G

```

```

<400> 84
gctggtagcc tatggcgtgg ccacggangg gctcctgagg cacgggacag tgacttccca 60
agtatcctgc gccgcgtctt ctaccgtccc tacctgcaga tcttcgggca gattccccag 120
gaggacatgg acgtggccct catggagcac agcaactgct cgtcggagcc cggcttctgg 180
gcacacctct ctggggccca ggccgggcacc tgcgtctccc agtatgccaa ctggctgggtg 240
gtgctgctcc tcttcattct cctgctcgtg gccaaacatcc tgctggtcac ttgctcattg 300
ccatgttcag ttacacattc ggcaaagtac agggcaacag cnatctctac tgggaaggcc 360
agcgttncgg cctcatccgg 380

```

```

<210> 85
<211> 481
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(481)
<223> n = A,T,C or G

```

```

<400> 85
gagttagctc ctccacaacc ttgatgaggt cgtctgcagt ggctctctgc ttcataccgc 60
tnccatcgct atactgtagg ttggccacca cctcctgcat cttggggcgg ctaatatcca 120
ggaaactctc aatcaagtca ccgtcnatna aacctgtggc tggttctgtc ttccgctcgg 180
tgtgaaagga tctccagaag gagtgtctga tcttccccac acttttgatg actttattga 240
gtcgattctg catgtccagc aggaggttgt accagctctc tgacagttag gtcaccagcc 300
ctatcatgcc nttgaacgtg ccgaagaaca ccgagccttg tgtgggggggt gnagtctcac 360
ccagattctg cattaccaga nagccgtggc aaaaganatt gacaactcgc ccaggngaa 420
aaagaacacc tcctggaagt gctngccgct cctcgtccnt tggtggnnng gcntnccctt 480
t 481

```

```

<210> 86
<211> 472
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(472)
<223> n = A,T,C or G

```

```

<400> 86

```

```

aacatcttcc tgtataatgc tgtgtaatat cgatccgatn ttgtctgctg agaattcatt      60
acttggaaaa gcaacttnaa gcctggacac tggattataa attcacaata tgcaacacct      120
ccctattcac acctgtttaa agggcgctaa gcatttttga ttcaacatct ttttttttga      180
cacaagtcgg aaaaaagcaa aagtaaacag ttnttaattt gttagccaat tcactttctt      240
catgggacag agccatttga tttaaaaagc aaattgcata atattgagct ttggggagctg      300
atatntgagc ggaagantag cctttctact tcaccagaca caactccttt catattggga      360
tgtnnacnaa agttatgtct cttacagatg ggatgctttt gtggcaattc tg              420

```

```

<210> 87
<211> 413
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(413)
<223> n = A,T,C or G

```

```

<400> 87
agaaaccagt atctctnaaa acaacctctc ataccttggt gacctaatTT tgtgtgctg      60
tgtgtgtgct cgcataattat atagacaggc acatcttttt tacttttTga aaagcttatg      120
cctcttttgg atctatatct gtgaaagtTt taatgatctg ccataaatgtc ttggggacct      180
ttgtcttctg tgtaaatggT actagagaaa acacctatnt tatgagtcaa tctagttngt      240
tttattcgac atgaaggaaa tttccagatn acaacactna caaactctcc cttgactagg      300
ggggacaaaag aaaagcnaaa ctgaacatna gaaacaattn cctgggtgaga aattncataa      360
acagaaattg ggtngtatat tgaaananng catcattnaa acgttttttt ttt              413

```

```

<210> 88
<211> 448
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(448)
<223> n = A,T,C or G

```

```

<400> 88
cgcagcgggt cctctctatc tagctccagc ctctcgctg cccactccc cgcgtcccgc      60
gtcctagccn accatggcgg ggcctctgct cgccccgctg ctctctgctg ccactcctggc      120
cgtggccctg gccgtgagcc ccgcggccgg ctccagtccc ggcaagccgc cgcgcctggt      180
gggaggccca tggaccccg cgtggaagaag aagggtgtgct gcgtgcactg gactttgccc      240
tcggcnanta caacaaaccc gcaacnactt ttaccnagcn cgcgtctgag gttgtgccgc      300
cccaancaa tttgtactng gggtaantaa ttcttggaag ttgaacctg gccaaacnng      360
tttaccagaa ccnagccaat tngaacaatt nccctccat aacagcccct tttaaaaagg      420
gaancantcc tgnctctttc caaatTTt              448

```

```

<210> 89
<211> 463
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature

```

&lt;222&gt; (1)...(463)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 89

gaattttgtg cactggccac tgtgatggaa ccattgggcc aggatgcttt gagtttatca	60
gtagtgattc tgccaaagtt ggtgtttaa catgagtatg taaaagtca aaaaattagc	120
agaggcttag gtctgcatat cagcagacag tttgtccgtg tattttgtag ccttgaagtt	180
ctcagtaca agttntttct gatgcgaagt tctnattcca gtgttttagt cctttgcatc	240
tttnatgttn agacttgctt ctntnaaatt gcttttgtnt tctgcaggta ctatctgtgg	300
ttaacaacaaa tagaannact tctctgcttn gaanatttga atatcttaca tctnaaaatn	360
aattctctcc ccatannaaa acccangccc ttggganaat ttgaaaaang gntccttcnn	420
aattcnnana anttcagntn tcatacaaca naacngganc ccc	463

&lt;210&gt; 90

&lt;211&gt; 400

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(400)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 90

agggattgaa ggtctntnt actgtcggac tgttcanca ccaactctac aagttgctgt	60
cttcactca ctgtctgtaa gcntnttaac ccagactgta tcttcataaa tagaacaat	120
tcttcaccag tcacatcttc taggaccttt ttggattcag ttagtataag ctctccact	180
tcctttgtta agacttcac tggtaaaagtc ttaagttttg tagaaaggaa ttttaattgt	240
cgttctctaa caatgtcttc tccttgaagt atttggtga acaaccacc tnaagtcct	300
ttgtgcattc attttaaata tacttaatag ggcattggtn cactaggtta aattctgcga	360
gagtcattct tctgcaaaag ttgcgttagt atatctgcc	400

&lt;210&gt; 91

&lt;211&gt; 480

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(480)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 91

gagctcggat ccaataatct ttgtctgagg gcagcacaca tatncagtgc catggnaact	60
ggtctacccc acatgggagc agcatgccgt agntatataa ggtcattccc tgagtcagac	120
atgcctcttt gactaccgtg tgccagtgtt ggtgattctc acacacctcc nncgcctctt	180
tgtggaaaaa ctggcacttg nctggaacta gcaagacatc acttacaatc tcaccacga	240
gacacttgaa aggtgttaaca aagcgactct tgcattgtct tttgtccctc cggcaccagt	300
tgtcaatact aacccgctgg tttgcctcca tcacatttgt gatctgtagc tctggataca	360
tctcctgaca gtactgaaga acttcttctt ttgtttcaaa agcaactctt ggtgcctgtt	420
ngatcagggt cccatttccc agtccgaatg ttcacatggc atatnttact tcccacaaaa	480

&lt;210&gt; 92

&lt;211&gt; 477

&lt;212&gt; DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(477)

<223> n = A,T,C or G

<400> 92

atacagccca	natccccacca	cgaagatgcg	cttgttgact	gagaacctga	tgcggtcact	60
gggtcccgcgtg	tagccccagc	gactctccac	ctgctggaag	cggttgatgc	tgcactccct	120
cccacgcagg	cagcagcggg	gccggtcaat	gaactccact	cgtggcttg	gggttgacggt	180
taantgcagg	aagaggctga	ccacctcgcg	gtccaccagg	atgcccgaact	gtgcgggacc	240
tgcagcgaaa	ctcctcgatg	gtcatgagcg	ggaagcgaat	gangccagg	gccttgccca	300
gaaccttccg	cctgttctct	ggcgtcacct	gcagctgctg	ccgctnacac	tcggcctcgg	360
accagcggac	aaacggcggt	gaacagccgc	acctcacgga	tgcccantgt	gtcgcgctcc	420
aggaacggcn	ccagcgtgtc	cagggtcaatg	tcggtgaanc	ctccgcgggt	aatggcg	477

<210> 93

<211> 377

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(377)

<223> n = A,T,C or G

<400> 93

gaacggctgg	accttgcctc	gcatttgtct	gctggcagga	ataccttggc	aagcagctcc	60
agtccgagca	gccccagacc	gctgccgccc	gaagctaagc	ctgcctctgg	ccttccccctc	120
cgccctcaatg	cagaaccant	agtgaggagca	ctgtgttttag	agttaagagt	gaacactgtn	180
tgattttact	tgggaatttc	ctctgttata	tagcttttcc	caatgcta	ttccaaacaa	240
caacaacaaa	ataacatggt	tgctgtttna	gttgataaaa	agtangtgat	tctgtatnta	300
aagaaaatat	tactgttaca	tatactgctt	gcaanttctg	tatttattgg	tnctctggaa	360
ataaatatat	tattaaa					377

<210> 94

<211> 495

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(495)

<223> n = A,T,C or G

<400> 94

ccctttgagg	ggtttagggc	cagttcccag	tggagaagaa	aggccaggag	aantgcgtgc	60
cgagctgang	cagatttccc	acagtgaacc	cagagcccctg	ggctatagtc	tctgaccctc	120
ccaaggaaag	accaccttct	ggggacatgg	gctggagggc	aggacctaga	ggcaccaagg	180
gaaggcccca	ttccggggct	gttccccgag	gaggaaggga	aggggctctg	tgtgcccccc	240
acgaggaana	ggccctgant	cctgggatca	nacacccctt	cacgtgtatc	cccacacaaa	300
tgcaagctca	ccaaggtccc	ctctcagtcc	cttccctaca	ccctgaacgg	nactggccc	360
acaccacccc	agancancca	cccgccatgg	ggaatgtntc	caaggaaatc	cngggcaacg	420
tggactctng	tccnnaagg	gggcagaatc	tccaatagan	gganngaacc	cttgctnana	480

aaaaaaaaa aaaaa

495

&lt;210&gt; 95

&lt;211&gt; 472

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(472)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 95

ggttacttgg	tttcattgcc	accacttagt	ggatgtcatt	tagaaccatt	ttgtctgctc	60
cctctggaag	ccttgcgcag	agcggacttt	gtaattgttg	gagaataact	gctgaatttt	120
tagctgtttt	gagttgatcc	gcaccactgc	accacaactc	aatatgaaaa	ctatttnact	180
tatttattat	cttgtgaaaa	gtatacaatg	aaaattttgt	tcatactgta	tttatcaagt	240
atgatgaaaa	gcaatagata	tatatctctt	tattatgtn	aattatgatt	gccattatta	300
atcggcaaaa	tgtggagtgt	atgttctctt	cacagtaata	tatgcctttt	gtaacttcac	360
ttgggtattt	tattgtaaat	gaattacaaa	attcttaatt	taagaaaaatg	gtangttata	420
tttanttcan	taatttcttt	ccttgtttac	gttaattttg	aaaagaatgc	at	472

&lt;210&gt; 96

&lt;211&gt; 476

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(476)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 96

ctgaagcatt	tcttcaaact	tntctacttt	tgctcattgat	acctgtagta	agttgacaat	60
gtggtgaaat	ttcaaaaatta	tatgtaactt	ctactagtgtt	tactttctcc	cccaagtctt	120
ttttaactca	tgattttttac	acacacaatc	cagaacttat	tatatagcct	ctaagtcttt	180
attcttcaca	gtagatgatg	aaagagtcct	ccagtgtctt	gngcanaatg	ttctagntat	240
agctggatac	atacngtggg	agttctataa	actcatacct	cagtgggact	naaccaaaaat	300
tgtgttagtc	tcaattccta	ccacactgag	ggagcctccc	aaatcactat	attcttatct	360
gcagggtact	ctccagaaaa	acngacaggg	caggcttgca	tgaaaaagtn	acatctgcgt	420
tacaaaagtc	atcttctcta	nangtctgtn	aaggaacaat	ttaatcttct	agcttt	476

&lt;210&gt; 97

&lt;211&gt; 479

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(479)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 97

actctttcta	atgctgatat	gatcttgagt	ataagaatgc	atatgtcact	agaatggata	60
aaataatgct	gcaaaacttaa	tgttcttatg	caaaaatggaa	cgctaatagaa	acacagctta	120

caatcgcaaa	tcaaaactca	caagtgtctca	tctgtttag	atttagtgta	ataagactta	180
gatttgcttc	cttcggatat	gattgtttct	canatcttg	gcaatnttc	ttagtcaaat	240
caggctacta	gaattctgtt	attggatatn	tgagagcatg	aaatttttaa	naatacactt	300
gtgattatna	aattaatcac	aaatttcact	tatactgct	atcagcagct	agaaaaacat	360
ntnnttttta	natcaaagta	ttttgtgttt	ggaantgttn	aaatgaaatc	tgaatgtggg	420
ttnatctta	ttttttcccn	gacnactant	tnctttttta	gggnctattc	tganccatc	479

&lt;210&gt; 98

&lt;211&gt; 461

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 98

agtgacttgt	cctccaacaa	aaccccttga	tcaagtttgt	ggcactgaca	atcagaccta	60
tgctagtctc	tgtcatctat	tcgctactaa	atgcagactg	gaggggacca	aaaaggggca	120
tcaactccag	ctggattatt	ttggagcctg	caaatctatt	cctacttgta	cggactttga	180
agtgattcag	tttccctctac	ggatgagaga	ctggctcaag	aatacctcca	tcgagcttta	240
tgaagccact	ctgaacacgc	tggttatcta	gatgagaaca	gagaaataaa	gtcagaaaat	300
ttacctggag	aaaagaggct	ttggctgggg	accatcccat	tgaaccttct	cttaaggact	360
ttaagaaaaa	ctaccacatg	ttgtgtatcc	tggtgccggc	cgtttatgaa	ctgaccaccc	420
tttggataaa	tcttgacgct	cctgaacttg	ctcctctgcg	a		461

&lt;210&gt; 99

&lt;211&gt; 171

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 99

gtggccgcgc	gcagggtgtt	cctcgtaccg	caggggcccc	tccttcccc	aggcgctccct	60
cgggcgctct	gcgggcccga	ggaggagcgg	ctggcggtg	gggggagtg	gacccacccct	120
cggtgagaaa	agccttctct	agcgatctga	gaggcggtgc	ttgggggtac	c	171

&lt;210&gt; 100

&lt;211&gt; 269

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 100

cggccgcaag	tgcaactcca	gctggggccg	tgccggacga	gattctgcca	gcagttggtc	60
cgactgcgac	gacggcgccg	gcgacagtcg	caggtgcagc	gcgggcgcct	ggggtcttgc	120
aaggctgagc	tgacgcgcga	ggggtcgtgt	cacgtcccac	gaccttgacg	ccgtcgggga	180
cagccggaac	agagcccggt	gaagcgggag	gcctcgggga	gccccctcgg	aagggcgcc	240
cgagagatac	gcaggtgcag	gtggccgcgc				269

&lt;210&gt; 101

&lt;211&gt; 405

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 101

tttttttttt	ttttggaatc	tactgcgagc	acagcaggtc	agcaacaagt	ttattttgca	60
gctagcaagg	taacagggta	gggcatgggt	acatgttccg	gtcaacttcc	tttgtcgtgg	120
ttgattggtt	tgtctttatg	ggggcggggg	ggggtagggg	aaacgaagca	aataacatgg	180
agtggtgtgc	ccctccctgt	agaacctgg	tacaaaagct	ggggcagttc	acctggctcg	240
tgaccgtcat	tttcttgaca	tcaatgttat	tagaagtcag	gatattcttt	agagagtcca	300

ctgttcttggga	gggagatttag	ggtttcttgc	caaatccaac	aaaatccact	gaaaaagtgtg	360
gatgatcagt	acgaataaccg	aggcatattc	tcataatcggt	ggcca		405

<210> 102  
 <211> 470  
 <212> DNA  
 <213> Homo sapien

<400> 102						
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ggcacttaat	ccattttttat	ttcaaaatgt	ctacaaattt	aatcccat	tacgggtattt	120
tcaaaatcta	aattattcaa	attagccaaa	tccttaccaa	ataataccca	aaaatcaaaa	180
atatacttct	ttcagcaaac	ttgttacata	aattaaaaaa	atatatacgg	ctgggtgtttt	240
caaagtacaa	ttactttaac	actgcaaaaca	ttttaaggaa	ctaaaaataaa	aaaaaacact	300
ccgcaagggt	taaaggggaa	aacaaattct	tttacaacac	cattataaaa	atcatatctc	360
aaatcttagg	ggaatatata	cttcacacgg	gatcttaact	tttactcact	ttgtttattt	420
ttttaaacca	ttgtttgggc	ccaacacaa	ggaatcccc	ctggactagt		470

<210> 103  
 <211> 581  
 <212> DNA  
 <213> Homo sapien

<400> 103						
tttttttttt	ttttttttga	ccccctctt	ataaaaaaca	agttaccatt	ttattttact	60
tacacatatt	tattttataa	ttgggtattag	atattcaaaa	ggcagctttt	aaaatcaaac	120
taaatggaaa	ctgccttaga	tacataattc	ctaggaatta	gcttaaaatc	tgccctaaagt	180
gaaaatcttc	tctagctctt	ttgactgtaa	atttttgact	cttgtaaaac	atccaaatc	240
atttttcttg	tttttaaaat	tatctaattc	ttccattttt	tccttatctc	aagtcaattt	300
gttctcttag	cctcatttcc	tagctcttat	ctactattag	taagtggctt	ttttccataa	360
agggaaaaaa	ggaagagaaa	tggcacacaa	aacaaacatt	ttatattcat	atttctacct	420
acgttaataa	aatagcattt	tgtgaagcca	gctcaaaaga	aggcttagat	ccttttatgt	480
ccattttagt	cactaaacga	tatcaaagt	ccagaatgca	aaagggttgt	gaacatttat	540
tcaaaagcta	atataagata	tttcacatac	tcattctttc	g		581

<210> 104  
 <211> 578  
 <212> DNA  
 <213> Homo sapien

<400> 104						
tttttttttt	tttttttttt	tttttctctt	cttttttttt	gaaatgagga	tcgagttttt	60
cactctctag	atagggcatg	aagaaaactc	atctttccag	ctttaaaaa	acaatcaaat	120
ctcttatgct	atatcatatt	ttaagttaaa	ctaagtgtc	actggcttat	cttctccctga	180
aggaaatctg	ttcattcttc	tcattcatat	agttatatca	agtactacct	tgcatattga	240
gagggttttc	ttctcttatt	acacatatat	ttccatgtga	atttgatca	aacctttatt	300
ttcatgcaaa	ctagaaaata	atgtttcttt	tgcataagag	aagagaacaa	tatagcatta	360
caaaactgct	caaattgttt	gttaagttat	ccattataat	tagttggcag	gagctaatac	420
aaatcacatt	tacgacagca	ataataaaac	tgaagtacca	gttaaatatc	caaaaataatt	480
aaaggaacat	tttttagctg	ggtataatta	gctaattcac	tttacaagca	tttattagaa	540
tgatttcaca	tggtattatt	cctagcccaa	cacaatgg			578

<210> 105  
 <211> 538  
 <212> DNA



&lt;213&gt; Homo sapien

&lt;400&gt; 105

tttttttttt	tttttcagta	ataatcagaa	caatatttat	ttttatattt	aaaattcata	60
gaaaagtgcc	ttacatttaa	taaaagtttg	ttttctcaaag	tgatcagagg	aattagatat	120
gtcttgaaca	ccaatattaa	tttgaggaaa	atacaccaaa	atacattaag	taattatttt	180
aagatcatag	agcttgtaag	tgaaaagata	aaatttgacc	tcagaaactc	tgagcattaa	240
aaatccacta	ttagcaaata	aattactatg	gacttcttgc	tttaattttg	tgatgaatat	300
ggggtgtcac	tggtaaacca	acacattctg	aaggatacat	tacttagtga	tagattctta	360
tgtactttgc	taatacgtgg	atatgagttg	acaagtttct	ctttcttcaa	tcgtttaagg	420
ggcgagaaat	gaggaagaaa	agaaaaggat	tacgcatact	gttctttcta	tggaaggatt	480
agatatgttt	cctttgccaa	tattaaaaaa	ataataatgt	ttactactag	tgaaaccc	538

&lt;210&gt; 106

&lt;211&gt; 473

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 106

tttttttttt	ttttttagtc	aagtctctat	ttttattata	attaaagtct	tggtcatttc	60
atttattagc	tctgcaactt	acatatattaa	attaaagaaa	cgttttagac	aactgtacaa	120
tttataaatg	taagggtgcc	ttattgagta	atatattcct	ccaagagtgg	atgtgtccct	180
tctccacca	actaatgaac	agcaacatta	gtttaatttt	attagtagat	atacactgct	240
gcacaacgta	attctcttct	ccatcccat	gtgatattgt	gtatgtggtg	gagttggtag	300
aatgcatcac	aatctacaat	caacagcaag	atgaagctag	gctgggcttt	cggtgaaaat	360
agactgtgtc	tgtctgaatc	aaatgatctg	acctatcctc	ggtggaagaa	actcttcgaa	420
ccgcttcctc	aaaggcgctg	ccacatttgt	ggctctttgc	actgtttcca	aaa	473

&lt;210&gt; 107

&lt;211&gt; 1621

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 107

cgccatggca	ctgcagggca	tctcggtcac	ggagctgtcc	ggcctggccc	cgggcccgtt	60
ctgtgctatg	gtcctggctg	acttcggggc	gcgtgtggta	cgcgtggacc	ggcccggctc	120
ccgctacgac	gtgagccgct	tgggccgggg	caagcgctcg	ctagtgtctg	acctgaagca	180
gccgcgggga	gccgccgtgc	tgccgcgtct	gtgcaagcgg	tcggatgtgc	tgctggagcc	240
cttcgcgcgc	gggtgcatgg	agaaaactcca	gctggggcca	gagattctgc	agcgggaaaa	300
tcacaaggctt	atttatgccca	ggctgagtg	atttgccag	tcaggaagct	tctgcgggtt	360
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a 1621

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<210> 108
<211> 382
<212> PRT
<213> Homo sapien

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<400> 108
Met Ala Leu Gln Gly Ile Ser Val Met Glu Leu Ser Gly Leu Ala Pro
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Gly Pro Phe Cys Ala Met Val Leu Ala Asp Phe Gly Ala Arg Val Val
20 25 30
Arg Val Asp Arg Pro Gly Ser Arg Tyr Asp Val Ser Arg Leu Gly Arg
35 40 45
Gly Lys Arg Ser Leu Val Leu Asp Leu Lys Gln Pro Arg Gly Ala Ala
50 55 60
Val Leu Arg Arg Leu Cys Lys Arg Ser Asp Val Leu Leu Glu Pro Phe
65 70 75 80
Arg Arg Gly Val Met Glu Lys Leu Gln Leu Gly Pro Glu Ile Leu Gln
85 90 95
Arg Glu Asn Pro Arg Leu Ile Tyr Ala Arg Leu Ser Gly Phe Gly Gln
100 105 110
Ser Gly Ser Phe Cys Arg Leu Ala Gly His Asp Ile Asn Tyr Leu Ala
115 120 125
Leu Ser Gly Val Leu Ser Lys Ile Gly Arg Ser Gly Glu Asn Pro Tyr
130 135 140
Ala Pro Leu Asn Leu Leu Ala Asp Phe Ala Gly Gly Gly Leu Met Cys
145 150 155 160
Ala Leu Gly Ile Ile Met Ala Leu Phe Asp Arg Thr Arg Thr Asp Lys
165 170 175
Gly Gln Val Ile Asp Ala Asn Met Val Glu Gly Thr Ala Tyr Leu Ser
180 185 190
Ser Phe Leu Trp Lys Thr Gln Lys Ser Ser Leu Trp Glu Ala Pro Arg
195 200 205
Gly Gln Asn Met Leu Asp Gly Gly Ala Pro Phe Tyr Thr Thr Tyr Arg
210 215 220
Thr Ala Asp Gly Glu Phe Met Ala Val Gly Ala Ile Glu Pro Gln Phe
225 230 235 240
Tyr Glu Leu Leu Ile Lys Gly Leu Gly Leu Lys Ser Asp Glu Leu Pro
245 250 255
Asn Gln Met Ser Met Asp Asp Trp Pro Glu Met Lys Lys Lys Phe Ala
260 265 270
Asp Val Phe Ala Lys Lys Thr Lys Ala Glu Trp Cys Gln Ile Phe Asp
275 280 285
Gly Thr Asp Ala Cys Val Thr Pro Val Leu Thr Phe Glu Glu Val Val
290 295 300
His His Asp His Asn Lys Glu Arg Gly Ser Phe Ile Thr Ser Glu Glu
305 310 315 320
Gln Asp Val Ser Pro Arg Pro Ala Pro Leu Leu Leu Asn Thr Pro Ala

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325 330 335  
 Ile Pro Ser Phe Lys Arg Asp Pro Phe Ile Gly Glu His Thr Glu Glu  
 340 345 350  
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 355 360 365  
 Ser Asp Lys Ile Ile Glu Ser Asn Lys Val Lys Ala Ser Leu  
 370 375 380

<210> 109  
 <211> 1524  
 <212> DNA  
 <213> Homo sapien

<400> 109  
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 gccacggcgg gcacctgcgt ctcccagtat gccaaactgg tgggtgggtgct gctcctcgtc 600  
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 cagaggaataa aaaaaaaaaa aaaa 1524

<210> 110  
 <211> 3410  
 <212> DNA  
 <213> Homo sapien

<400> 110  
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cctgggcgtg	gggctgtgg	acttctgtgg	ccaggtgtgc	ttcactccac	tggaggccct	720
gctctctgac	ctcttccggg	accggacca	ctgtcgccag	gcctactctg	tctatgcctt	780
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aaaaaaaaara	aaaaaaaaaa	aaaaaaaaaa	aaaaaaataa	aaaaaaaaaa		3410

&lt;210&gt; 111

&lt;211&gt; 1289

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 111

```

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tgttacaatg ttaaaaaaaaa aaaaaaaaaa      1269

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&lt;210&gt; 112

&lt;211&gt; 315

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 112

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Met Val Phe Thr Val Arg Leu Leu His Ile Phe Thr Val Asn Lys Gln
1      5      10      15
Leu Gly Pro Lys Ile Val Ile Val Ser Lys Met Met Lys Asp Val Phe
20     25     30
Phe Phe Leu Phe Phe Leu Gly Val Trp Leu Val Ala Tyr Gly Val Ala
35     40     45
Thr Glu Gly Leu Leu Arg Pro Arg Asp Ser Asp Phe Pro Ser Ile Leu
50     55     60
Arg Arg Val Phe Tyr Arg Pro Tyr Leu Gln Ile Phe Gly Gln Ile Pro
65     70     75     80
Gln Glu Asp Met Asp Val Ala Leu Met Glu His Ser Asn Cys Ser Ser
85     90     95
Glu Pro Gly Phe Trp Ala His Pro Pro Gly Ala Gln Ala Gly Thr Cys
100    105    110
Val Ser Gln Tyr Ala Asn Trp Leu Val Val Leu Leu Val Ile Phe
115    120    125
Leu Leu Val Ala Asn Ile Leu Leu Val Asn Leu Leu Ile Ala Met Phe
130    135    140
Ser Tyr Thr Phe Gly Lys Val Gln Gly Asn Ser Asp Leu Tyr Trp Lys
145    150    155    160
Ala Gln Arg Tyr Arg Leu Ile Arg Glu Phe His Ser Arg Pro Ala Leu
165    170    175
Ala Pro Pro Phe Ile Val Ile Ser His Leu Arg Leu Leu Leu Arg Gln
180    185    190
Leu Cys Arg Arg Pro Arg Ser Pro Gln Pro Ser Ser Pro Ala Leu Glu

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      195              200              205
His Phe Arg Val Tyr Leu Ser Lys Glu Ala Glu Arg Lys Leu Leu Thr
  210              215              220
Trp Glu Ser Val His Lys Glu Asn Phe Leu Leu Ala Arg Ala Arg Asp
  225              230              235              240
Lys Arg Glu Ser Asp Ser Glu Arg Leu Lys Arg Thr Ser Gln Lys Val
      245              250              255
Asp Leu Ala Leu Lys Gln Leu Gly His Ile Arg Glu Tyr Glu Gln Arg
      260              265              270
Leu Lys Val Leu Glu Arg Glu Val Gln Gln Cys Ser Arg Val Leu Gly
      275              280              285
Trp Val Ala Glu Ala Leu Ser Arg Ser Ala Leu Leu Pro Pro Gly Gly
      290              295              300
Pro Pro Pro Pro Asp Leu Pro Gly Ser Lys Asp
  305              310              315

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<210> 113
<211> 553
<212> PRT
<213> Homo sapien

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      <400> 113
Met Val Gln Arg Leu Trp Val Ser Arg Leu Leu Arg His Arg Lys Ala
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Gln Leu Leu Leu Val Asn Leu Leu Thr Phe Gly Leu Glu Val Cys Leu
      20              25              30
Ala Ala Gly Ile Thr Tyr Val Pro Leu Leu Leu Glu Val Gly Val
      35              40              45
Glu Glu Lys Phe Met Thr Met Val Leu Gly Ile Gly Pro Val Leu Gly
      50              55              60
Leu Val Cys Val Pro Leu Leu Gly Ser Ala Ser Asp His Trp Arg Gly
      65              70              75              80
Arg Tyr Gly Arg Arg Arg Pro Phe Ile Trp Ala Leu Ser Leu Gly Ile
      85              90              95
Leu Leu Ser Leu Phe Leu Ile Pro Arg Ala Gly Trp Leu Ala Gly Leu
      100              105              110
Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu Ala Leu Leu Ile Leu Gly
      115              120              125
Val Gly Leu Leu Asp Phe Cys Gly Gln Val Cys Phe Thr Pro Leu Glu
      130              135              140
Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro Asp His Cys Arg Gln Ala
      145              150              155              160
Tyr Ser Val Tyr Ala Phe Met Ile Ser Leu Gly Gly Cys Leu Gly Tyr
      165              170              175
Leu Leu Pro Ala Ile Asp Trp Asp Thr Ser Ala Leu Ala Pro Tyr Leu
      180              185              190
Gly Thr Gln Glu Glu Cys Leu Phe Gly Leu Leu Thr Leu Ile Phe Leu
      195              200              205
Thr Cys Val Ala Ala Thr Leu Leu Val Ala Glu Glu Ala Ala Leu Gly
      210              215              220
Pro Thr Glu Pro Ala Glu Gly Leu Ser Ala Pro Ser Leu Ser Pro His
      225              230              235              240
Cys Cys Pro Cys Arg Ala Arg Leu Ala Phe Arg Asn Leu Gly Ala Leu
      245              250              255
Leu Pro Arg Leu His Gln Leu Cys Cys Arg Met Pro Arg Thr Leu Arg

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      260      265      270
Arg Leu Phe Val Ala Glu Leu Cys Ser Trp Met Ala Leu Met Thr Phe
      275      280      285
Thr Leu Phe Tyr Thr Asp Phe Val Gly Glu Gly Leu Tyr Gln Gly Val
      290      295      300
Pro Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg His Tyr Asp Glu Gly
      305      310      315      320
Val Arg Met Gly Ser Leu Gly Leu Phe Leu Gln Cys Ala Ile Ser Leu
      325      330      335
Val Phe Ser Leu Val Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg
      340      345      350
Ala Val Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala
      355      360      365
Thr Cys Leu Ser His Ser Val Ala Val Val Thr Ala Ser Ala Ala Leu
      370      375      380
Thr Gly Phe Thr Phe Ser Ala Leu Gln Ile Leu Pro Tyr Thr Leu Ala
      385      390      395      400
Ser Leu Tyr His Arg Glu Lys Gln Val Phe Leu Pro Lys Tyr Arg Gly
      405      410      415
Asp Thr Gly Gly Ala Ser Ser Glu Asp Ser Leu Met Thr Ser Phe Leu
      420      425      430
Pro Gly Pro Lys Pro Gly Ala Pro Phe Pro Asn Gly His Val Gly Ala
      435      440      445
Gly Gly Ser Gly Leu Leu Pro Pro Pro Ala Leu Cys Gly Ala Ser
      450      455      460
Ala Cys Asp Val Ser Val Arg Val Val Val Gly Glu Pro Thr Glu Ala
      465      470      475      480
Arg Val Val Pro Gly Arg Gly Ile Cys Leu Asp Leu Ala Ile Leu Asp
      485      490      495
Ser Ala Phe Leu Leu Ser Gln Val Ala Pro Ser Leu Phe Met Gly Ser
      500      505      510
Ile Val Gln Leu Ser Gln Ser Val Thr Ala Tyr Met Val Ser Ala Ala
      515      520      525
Gly Leu Gly Leu Val Ala Ile Tyr Phe Ala Thr Gln Val Val Phe Asp
      530      535      540
Lys Ser Asp Leu Ala Lys Tyr Ser Ala
      545      550

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&lt;210&gt; 114

&lt;211&gt; 241

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 114

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Met Gln Cys Phe Ser Phe Ile Lys Thr Met Met Ile Leu Phe Asn Leu
  1          5          10          15
Leu Ile Phe Leu Cys Gly Ala Ala Leu Leu Ala Val Gly Ile Trp Val
      20      25      30
Ser Ile Asp Gly Ala Ser Phe Leu Lys Ile Phe Gly Pro Leu Ser Ser
      35      40      45
Ser Ala Met Gln Phe Val Asn Val Gly Tyr Phe Leu Ile Ala Ala Gly
      50      55      60
Val Val Val Phe Ala Leu Gly Phe Leu Gly Cys Tyr Gly Ala Lys Thr
      65      70      75      80
Glu Ser Lys Cys Ala Leu Val Thr Phe Phe Ile Leu Leu Leu Ile

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[illegible]

<210> 115

<211> 366

<212> DNA

<213> Homo sapien

<400> 115

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actggtagaa	aaacatctga	agagctagtc	tatcagcatt	tgacaggtga	atttgatggt	240
tctcagaacc	atttcacca	gacagcctgt	tctatctctg	ttaataaat	tagtttgggt	300
tctctacatg	cataacaaac	cctgctccaa	tctgtcacat	aaaagtctgt	gacttgaagt	360
ttagtc						366

<210> 116

<211> 282

<212> DNA

<213> Homo sapien

<220>

<221> misc feature

<222> (1) ... (282)

<223> n = A,T,C or G

<400> 116

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gagaaatgag	atnaaacaca	atnttataaa	gtctacttag	agaagatcaa	gtgacctcaa	120
agactttact	attttcatat	ttaaagacac	atgatttatc	ctattttagt	aactcggttc	180
atacgtttaa	caaaggataa	tgtgaacagc	agagaggatt	tgtggcga	aaatctatgt	240
tcaactctga	actactctana	tcacagacat	ttctattctt	tt		282

<210> 117

<211> 305



<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(305)  
<223> n = A,T,C or G

<400> 117  
acacatgtcg cttcactgcc ttcttagatg cttctggtca acatanagga acagggacca 60  
tatttatcct ccctcctgaa acaattgcaa aataanacaa aatatatgaa acaattgcaa 120  
aataaggcaa aatatatgaa acaacaggtc tcgagatatt ggaaatcagt caatgaagga 180  
tactgatccc tgatcactgt cctaatgcag gatgtgggaa acagatgagg tcacctctgt 240  
gactgcccc gcttactgcc tgtagagagt ttctangctg cagttcagac agggagaaat 300  
tgggt 305

<210> 118  
<211> 71  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(71)  
<223> n = A,T,C or G

<400> 118  
accaagggtg ntgaatctct gacgtgggga tctctgattc ccgcacaatc tgagtggaaa 60  
aantcctggg t 71

<210> 119  
<211> 212  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(212)  
<223> n = A,T,C or G

<400> 119  
actccggttg gtgtcagcag cactgtggcat tgaacatngc aatgtggagc ccaaaccaca 60  
gaaaatgggg tgaattggc caactttcta tnaacttatg ttggcaantt tgccaccaac 120  
agtaagctgg cccttctaataaaaagaaat tgaaaggttt ctactaanc ggaattaant 180  
aatggantca aganactccc aggcctcagc gt 212

<210> 120  
<211> 90  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(90)  
<223> n = A,T,C or G

```

<400> 120
actcgttgca natcaggggc cccccagagt caccgttgca ggagtccttc tggctcttgc
ctccgccggc gcagaacatg ctgggggtgtg
60
90

<210> 121
<211> 218
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(218)
<223> n = A,T,C or G

<400> 121
tgtancgtga anacgacaga naggggtgtc aaaaatggag aanccttgaa gtcattttga
gaataagatt tgctaaaaga ttgggggcta aaacatgggt attggggagac atttctgaag
atatncangt aaattangga atgaattcat ggttcttttg ggaattcctt tacgatngcc
agcatanact tcatgtgggg atancagcta cccttgta
60
120
180
218

<210> 122
<211> 171
<212> DNA
<213> Homo sapien

<400> 122
taggggtgta tgcaactgta aggacaaaaa ttgagactca actggcttaa ccaataaagg
catttgtagt ctcatggaac aggaagtcgg atgggtgggc atcttcagtg ctgcatgagt
caccaccccg gcggggtcat ctgtgccaca ggtccctgtt gacagtgccg t
60
120
171

<210> 123
<211> 76
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(76)
<223> n = A,T,C or G

<400> 123
tgtagcgtga agacnacaga atgggtgtgtg ctgtgctatc caggaacaca tttattatca
ttatcaanta ttgtgt
60
76

<210> 124
<211> 131
<212> DNA
<213> Homo sapien

<400> 124
acctttcccc aagccaatg tctctgtgtc taactggccg gctgcaggac agctgcaatt
caatgtgctg ggtcatatgg agggggaggag actctaaaat agccaatttt atttctcttg
ttaagatttg t
60
120
131

```

<210> 125  
 <211> 432  
 <212> DNA  
 <213> Homo sapien

<400> 125  
 actttatcta ctggctatga aatagatggg ggaaaattgc gttaccaact ataccactgg 60  
 cttgaaaaag aggtgatagc tcttcagagg acttgtgact tttgctcaga tgctgaagaa 120  
 ctacagtcctg catttggcag aaatgaagat gaatttggat taaatgagga tgctgaagat 180  
 ttgcctcacc aaacaaaagt gaaacaactg agagaaaatt ttcaggaaaa aagacagtgg 240  
 ctcttgaagt atcagtcact tttgagaatg tttcttagtt actgcatact tcatggatcc 300  
 catggtgggg gtcttgcatc tgtaagaatg gaattgattt tgcttttgca agaatctcag 360  
 caggaaacat cagaaccact attttctagc cctctgtcag agcaaaccctc agtgcctctc 420  
 ctctttgctt gt 432

<210> 126  
 <211> 112  
 <212> DNA  
 <213> Homo sapien

<400> 126  
 acacaacttg aatagtaaaa tagaaactga gctgaaattt ctaattcact ttctaaccat 60  
 agtaagaatg atatttcccc ccagggatca ccaaatattt ataaaaattt gt 112

<210> 127  
 <211> 54  
 <212> DNA  
 <213> Homo sapien

<400> 127  
 accacgaaac cacaacaag atggaagcat caatccactt gccaaagcaca gcag 54

<210> 128  
 <211> 323  
 <212> DNA  
 <213> Homo sapien

<400> 128  
 acctcattag taattgtttt gttgtttcat ttttttctaa tgtctccctt ctaccagctc 60  
 acctgagata acagaatgaa aatggaagga cagccagatt tctcctttgc tctctgctca 120  
 ttctctctga agtctagggt acccattttg gggaccatt ataggcaata aacacagttc 180  
 ccaaagcatt tggacagttt cttgttgtgt tttagaatgg ttttcctttt tcttagcctt 240  
 ttcttgcaaa aggtcactc agtccttgc ttgctcagtg gactgggctc cccagggcct 300  
 aggtgcctt cttttccatg tcc 323

<210> 129  
 <211> 192  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (192)  
 <223> n = A,T,C or G

```

<400> 129
acatacatgt gtgtatatatt ttaaataatca cttttgtatc actctgactt ttttagcatac    60
tgaaaacaca ctaacataat ttntgtgaac catgatcaga tacaacccaa atcattcacc    120
tagcacattc atctgtgata naaagatagg tgaggtttcat ttccttcacg ttggccaatg    180
gataaacaaa gt                                     192

```

```

<210> 130
<211> 362
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(362)
<223> n = A,T,C or G

```

```

<400> 130
ccctttttta tgggaatgagt agactgtatg ttggaanatt tanccacaac ctctttgaca    60
tataatgacg caacaaaaag gtgctgttta gtcctatggt tcagtttatg cccttgacaa    120
gtttccattg tgttttgccg atcttctggc taatcgtggg atcctccatg ttattagtaa    180
ttctgtattc cattttgtta acgcctggga gatgtaacct gctangaggc taactttata    240
cttatttaaa agctcttatt ttgtggtcac taaaatggca atttatgtgc agcactttat    300
tgcagcagga agcagctgtg ggttggttgt aaagctcttt gctaattctta aaaagtaatg    360
gg                                     362

```

```

<210> 131
<211> 332
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(332)
<223> n = A,T,C or G

```

```

<400> 131
ctttttgaaa gatcgtgtcc actcctgttg acatcttggt ttaatggagt ttcccatgca    60
gtangactgg tatggttgca gctgtccaga taaaaacatt tgaagagctc caaaatgaga    120
gttctcccag gttcgccctg ctgctccaag tctcagcagc agcctctttt aggaggcatc    180
ttctgaacta gattaaggca gcttgtaa atctgatgtg ttgggttatt atccaactaa    240
cttccatctg ttatcactgg agaaaagcca gactcccan gacnggtacg gattgtgggc    300
atanaaggat tgggtgaagc tggcggtgtg gt                                     332

```

```

<210> 132
<211> 322
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(322)
<223> n = A,T,C or G

```

```

<400> 132
acttttgcca ttttgtatat ataaacaatc ttgggacatt ctctgaaaa ctagggtgtcc    60

```

```

agtggtctaag agaactcgat ttcaagcaat tctgaaagga aaaccagcat gacacagaat 120
ctcaaatccc caaacagggg ctctgtggga aaaatgaggg aggacctttg tatctcgggt 180
tttagcaagt taaaatgaan atgacaggaa aggcttattt atcaacaaag agaagagttg 240
ggatgcttct aaaaaaact ttggtagaga aaataggaat gctnaatcct aggggaagcct 300
gtaacaatct acaattgggtc ca 322

```

&lt;210&gt; 133

&lt;211&gt; 278

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(278)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 133

```

acaagccttc acaagtttaa ctaaaattggg attaatcttt ctgtanttat ctgcataatt 60
cttggttttc tttccatctg gctcctgggt tgacaatttg tggaaacaac tctattgcta 120
ctatttaaaa aaaatcacia atctttccct ttaagctatg ttnaattcaa actattcctg 180
ctattcctgt ttgtcacaag aaattatatt ttcaaaaata tgtnattttg ttgatgggt 240
ccacgaaac actaataaaa accacagaga ccagcctg 278

```

&lt;210&gt; 134

&lt;211&gt; 121

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(121)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 134

```

gtttanaaaa cttgttttagc tccatagagg aaagaatggt aaactttgta ttttaaaaca 60
tgattctctg aggttaaaact tgggtttcaa atgttatttt tacttgatt ttgcttttgg 120
t 121

```

&lt;210&gt; 135

&lt;211&gt; 350

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(350)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 135

```

acttanaacc atgcctagca catcagaatc cctcaaagaa catcagtata atcctatacc 60
atancaagtg gtgactgggt aagcgtgcga caaaggctcag ctggcacatt acttggtggtc 120
aaacttgata cttttgttct aagtaggaac tagtatacag tncctaggan tggtagctcca 180
gggtgccccc caactcctgc agccgctcct ctgtgccagn ccctgnaagg aactttcgct 240
ccacctcaat caagccctgg gccatgctac ctgcaatttg ctgaacaaac gtttgctgag 300
ttccaagga tgcaaaagcct ggtgctcaac tcctggggcg tcaactcagt 350

```

<210> 136  
 <211> 399  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(399)  
 <223> n = A,T,C or G

<400> 136  
 tgtaccgtga agacgacaga agttgcatgg cagggacagg gcaggggccga ggccagggtt 60  
 gctgtgattg tatccgaata ntccctcgtga gaaaagataa tgagatgacg tgagcagcct 120  
 gcagacttgt gtctgccttc aanaagccag acaggaaggc cctgcctgcc ttggctctga 180  
 cctggcggcc agccagccag ccacagggtg gcttcttcct tttgtggtga caacnccaag 240  
 aaaactgcag aggccccagg tcaggtgtga gtgggtangt gaccataaaa caccagggtgc 300  
 tcccaggaac ccggggcaaag gccatcccca cctacagcca gcatgcccac tggcgtgatg 360  
 ggtgcagang gatgaagcag ccagntgttc tgctgtggt 399

<210> 137  
 <211> 165  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(165)  
 <223> n = A,T,C or G

<400> 137  
 actggtgtgg tngggggtga tgctggtggt anaagttgan gtgacttcan gatggtgtgt 60  
 ggaggaagtg tgtgaacgta gggatgtaga ngttttggcc gtgctaaatg agcttcggga 120  
 ttggtggtc ccactggtgg tcactgtcat tgggtgggtt cctgt 165

<210> 138  
 <211> 338  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(338)  
 <223> n = A,T,C or G

<400> 138  
 actcactgga atgccacatt cacaacagaa tcagaggtct gtgaaaacat taatggctcc 60  
 ttaacttctc cagtaagaat cagggacttg aaatggaaac gttaacagcc acatgcccaa 120  
 tgctgggcag tctcccatgc cttccacagt gaaagggctt gaaaaaatc acatccaatg 180  
 tcattgtgtt ccagccacac caaaaggtgc ttggggtgga gggctggggg catananggt 240  
 cangcctcag gaagcctcaa gttccattca gctttgccac tgtacattcc ccatntttaa 300  
 aaaaactgat gccttttttt tttttttttg taaaattc 338

<210> 139  
 <211> 382

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 139

gggaatcttg gtttttggca tctggtttgc ctatagccga ggccactttg acagaacaaa	60
gaaagggact tcgagtaaga aggtgattta cagccagcct agtgcgccga gtgaaggaga	120
attcaaacag acctcgatcat tcctgggttg agcctgggtg gctcaccgcc tatcatctgc	180
atttgcctta ctacaggtgct accggactct ggccctgat gtctgtagtt tcacaggatg	240
ccttatttgt cttctacacc ccacagggcc ccctacttct tcggatgtgt ttttaataat	300
gtcagctatg tgcccatcc tccttcacgc cctccctccc tttcctacca ctgctgagtg	360
gcctggaact tgtttaaagt gt	382

&lt;210&gt; 140

&lt;211&gt; 200

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(200)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 140

accaaancct ctttctgttg tgttngattt tactataggg gtttngcttn ttctaaanat	60
acttttcatt taacancctt tgtaagtgt caggctgcac tttgctccat anaattattg	120
ttttcacatt tcaacttgta tgtgtttgtc tcttanagca ttggtgaaat cacatatttt	180
atattcagca taaaggagaa	200

&lt;210&gt; 141

&lt;211&gt; 335

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(335)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 141

actttatttt caaacactc atatgttgca aaaaacacat agaaaaataa agtttgggtg	60
gggtgctgac taaacttcaa gtcacagact tttatgtgac agattggagc agggtttgtt	120
atgcattgtag agaaccacaa ctaatttatt aaacaggata gaaacaggct gtctgggtga	180
aatggttctg agaaccatcc aattcacctg tcagatgctg atanactagc tcttcagatg	240
tttttctacc agttcagaga tnggttaatg actanttcca atggggaaaa agcaagatgg	300
attcacaaac caagtaattt taaacaaaga cactt	335

&lt;210&gt; 142

&lt;211&gt; 459

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(459)

&lt;223&gt; n = A,T,C or G

```

<400> 142
accagggttaa tattgccaca tatatccttt ccaattgcgg gctaaacaga cgtgtattta      60
gggttggtta aagacaaccc agcttaatat caagagaaat tgtgacctt catggagtat      120
ctgatggaga aaacactgag ttttgacaaa tcttatttta ttcagatagc agtctgatca      180
cacatgggtcc aacaacactc aaataataaa tcaaatatna tcagatgtta aagattggtc      240
ttcaaacatc atagccaatg atgccccgct tgcctataat ctctccgaca taaaaccaca      300
tcaacacctc agtggccacc aaaccattca gcacagcttc cttaactgtg agctgtttga      360
agctaccagt ctgagcacta ttgactatnt ttttcangct ctgaatagct ctagggatct      420
cagcangggg gggaggaacc agctcaacct tggcgtant                                459

```

<210> 143

<211> 140

<212> DNA

<213> Homo sapien

```

<400> 143
acatttcctt ccaccaagtc aggactcctg gcttctgtgg gagttcttat cacctgaggg      60
aaatccaac agtctctcct agaaaggaat agtgtcacca accccaccca tctccctgag      120
accatccgac ttccctgtgtg                                140

```

<210> 144

<211> 164

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(164)

<223> n = A,T,C or G

```

<400> 144
acttcagtaa caacatacaa taacaacatt aagtgtatat tgccatcttt gtcattttct      60
atctatacca ctctcccttc tgaaaaaan aatcactanc caatcactta tacaaaattg      120
aggcaattaa tccatatattg ttttcaataa ggaaaaaaag atgt                                164

```

<210> 145

<211> 303

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(303)

<223> n = A,T,C or G

```

<400> 145
acgtagacca tccaactttg tatttghta ggcacacatc cagnagcaat tcctaaacaa      60
actggagggt atttatacc aattatccca ttcattaaca tgccctcctc ctccaggctat      120
gcaggacagc tatcataagt cggcccaggc atccagatac taccatttgt ataaacttca      180
gtaggggagt ccatccaagt gacaggtcta atcaaaggag gaaatggaac ataagcccag      240
tagtaaaatn ttgcttagct gaaacagcca caaaagactt accgccgtgg tgattaccat      300
caa                                                303

```

<210> 146



<211> 327  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(327)  
 <223> n = A,T,C or G

<400> 146  
 actgcagctc aattagaagt ggtctctgac ttctcatcanc ttctccctgg gctccatgac 60  
 actggccttg agtgactcat tgctctgggt ggttgagaga gctcctttgc caacaggcct 120  
 ccaagtcagg gctgggattt gtttcccttc cacattctag caacaatatg ctggccactt 180  
 cctgaacagg gagggtgagg ggagccagca tggacaagc tgccactttc taaagtagcc 240  
 agacttgccc ctgggcctgt cacacctact gatgaccttc tgtgcctgca ggatggaatg 300  
 taggggtgag ctgtgtgact ctatgggt 327

<210> 147  
 <211> 173  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(173)  
 <223> n = A,T,C or G

<400> 147  
 acattgtttt ttgagataa agcattgana gagctctcct taacgtgaca caatggaagg 60  
 actggaacac ataccacat ctttgttctg agggataatt ttctgataaa gtcttgctgt 120  
 atattcaagc acatatgtta tatattattc agttccatgt ttatagcccta gtt 173

<210> 148  
 <211> 477  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(477)  
 <223> n = A,T,C or G

<400> 148  
 acaaccactt tatctcatcg aatttttaac caaaactcac tcaactgtgc tttctatcct 60  
 atgggatata ttatttgatg ctccatttca tcacacatat atgaataata cactcatact 120  
 gccctactac ctgctgcaat aatcacattc ccttcctgtc ctgaccctga agccattggg 180  
 gtggtcctag tggccatcag tccangcctg caccttgagc ccttgagctc cattgtctac 240  
 nccanccac ctacccgacc ccattcctct acacagctac ctccctgtc tctaacccca 300  
 tagattatnt ccaaatcag tcaattaagt tactattaac actctaccg acatgtccag 360  
 caccactggg aagccttctc cagccaacac acacacacac acacncacac acacacatat 420  
 ccaggcacag gctacctcat ctccacaatc acccctttaa ttaccatgct atgggtgg 477

<210> 149  
 <211> 207  
 <212> DNA

<213> Homo sapien

<400> 149

acagttgtat tataatatca agaaataaac ttgcaatgag agcattttaag agggaagaac	60
taacgtattt tagagagcca aggaaggttt ctgtggggag tgggatgtaa ggtggggcct	120
gatgataaat aagagtcagc caggtaagtg ggtgggtgtg tatgggcaca gtgaagaaca	180
tttcaggcag agggaacagc agtgaaa	207

<210> 150

<211> 111

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(111)

<223> n = A,T,C or G

<400> 150

accttgattt cattgctgct ctgatggaaa cccaactatc taatttagct aaaacatggg	60
cacttaaatg tggtcagtgt ttggacttgt taactantgg catctttggg t	111

<210> 151

<211> 196

<212> DNA

<213> Homo sapien

<400> 151

agcgcggcag gtcatatga acattccaga tacctatcat tactcgatgc tgttgataac	60
agcaagatgg ctttgaactc agggtcacca ccagctattg gaccttacta tgaaaaccat	120
ggataccaac cggaaaaccc ctatcccga cagcccactg tggteccac tgtctacgag	180
gtgcatccg ctcagt	196

<210> 152

<211> 132

<212> DNA

<213> Homo sapien

<400> 152

acagcacttt cacatgtaag aagggagaaa ttcctaaatg tagggagaaag ataacagAAC	60
cttccccttt tcactagtgt gtggaacct gatgctttat gttgacagga atagaaccag	120
gagggagtgt gt	132

<210> 153

<211> 285

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(285)

<223> n = A,T,C or G

<400> 153

acaanacca nganaggcca ctggccgtgg tgtcatggcc tccaaacatg aaagtgtcag	60
--	----

cttctgctct	tatgtctca	tctgacaact	ctttaccatt	tttatcctcg	ctcagcagga	120
gcacatcaat	aaagtccaaa	gtcttggaact	tggccttggc	ttggaggaag	tcatacaacac	180
cctggctagt	gagggtgcgg	cgccgctcct	ggatgacggc	atctgtgaag	tcgtgcacca	240
gtctgcaggc	cctgtggaag	cgccgtccac	acggagtnag	gaatt		285

&lt;210&gt; 154

&lt;211&gt; 333

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 154

accacagtcc	tggtgggcca	gggcttcctg	accctttctg	tgaaaagcca	tattatcacc	60
accccaaatt	tttccttaaa	tatctttaac	tgaagggggc	agcctcttga	ctgcaaagac	120
cctaagccgg	ttacacagct	aactcccact	ggccctgatt	tgtgaaattg	ctgctgcctg	180
attggcacag	gagtcgaagg	tgttcagctc	ccctcctccg	tggaacgaga	ctctgatttg	240
agtttcacaa	attctcgggc	cacctcgtca	ttgctcctct	gaaataaaat	cgggagaatg	300
gtcaggcctg	tctcatccat	atggatcttc	cgg			333

&lt;210&gt; 155

&lt;211&gt; 308

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(308)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 155

actggaaaata	ataaaaacca	catcacagtg	ttgtgtcaaa	gatcatcagg	gcatggatgg	60
gaaagtgcct	tggaactgt	aaagtgccta	acacatgac	gatgatcttt	gttataatat	120
ttgaatcacg	gtgcatacaa	actctcctgc	ctgctectcc	tgggccccag	ccccagcccc	180
atcacagctc	actgctctgt	tcattccaggc	ccagcatgta	gtggctgatt	cttcttggtc	240
gcttttagcc	tccanaagtt	tctctgaagc	caaccaaacc	tctangtgta	aggcatgctg	300
gccctggg						308

&lt;210&gt; 156

&lt;211&gt; 295

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 156

acctgtctcg	gtgcttgga	catattagga	actcaaaata	tgagatgata	acagtgcccta	60
ttattgatta	ctgagagAAC	tgtagacat	ttagtgaag	attttctaca	caggaaactga	120
gaataggaga	ttatgttttg	ccctcatatt	ctctcctatc	ctccttgccct	cattctatgt	180
ctaataatatt	ctcaatcaaa	taaggttagc	ataatcagga	aatcgaccaa	ataccaatat	240
aaaaccagat	gtctatcctt	aagattttca	aatagaaaac	aaattaacag	actat	295

&lt;210&gt; 157

&lt;211&gt; 126

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 157

acaagttaa	atagtgtgt	cactgtgcat	gtgctgaaat	gtgaaatcca	ccacatttct	60
-----------	-----------	------------	------------	------------	------------	----

```

gaagagcaaaa acaaatctctg tcatgtaatc tctatcttgg gtcgtgggta tatctgtccc 120
cttagt                                           126

```

```

<210> 158
<211> 442
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(442)
<223> n = A,T,C or G

```

```

<400> 158
accactggt cttggaaaca cccatcctta atacgatgat tttctgtcg tgtgaaaatg      60
aanccagcag gctgccctta gtcagtcctt ccttcagag aaaaagagat ttgagaaagt    120
gcctgggtaa ttaccatta atttctctcc ccaaactctc tgagtcttcc cttaatatct    180
ctggtggttc tgaccaaagc aggtcatggt ttgttgagca tttgggatcc cagtgaagta    240
natgtttgta gccttgcata cttagccctt cccacgcaca aacggagtgg cagagtgggtg    300
ccaaccctgt tttcccagtc cacgtagaca gattcacagt gcggaattct ggaagctgga    360
nacagagggg ctctttgcag agccgggact ctgagangga catgagggcc tctgcctctg    420
tgttcattct ctgatgtcct gt                                           442

```

```

<210> 159
<211> 498
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(498)
<223> n = A,T,C or G

```

```

<400> 159
acttccagggt aacgttggtt tttccgttga gcctgaactg atgggtgacg ttgtagggtc      60
tccaacaaga actgaggttg cagagcgggt aggggaagagt gctgttccag ttgcacctgg    120
gctgctgtgg actgtgtgtg atttctcact acggcccaag gttgtggaac tggcanaaaag    180
gtgtgttgtt gganttgagc tcgggcggct gtggtagggt gtgggctctt caacaggggc    240
tgctgtggtg ccgggagtgt aangtgttgt gtcacttgag cttggccagc tctggaaaagt    300
antanattct tctgaaggc cagcgttgtt ggagctggca ngggtcantg ttgtgtgtaa    360
cgaaccagtg ctgctgtggg tgggtgtana tcctccacaa agcctgaagt tatgggtgctn    420
tcaggtaana atgtggtttc agtgtccctg ggcnegtgtg gaaggttgta nattgtcacc    480
aagggaataa gctgtggtg                                           498

```

```

<210> 160
<211> 380
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(380)
<223> n = A,T,C or G

```

```

<400> 160

```

```

acctgcattc agcttccctg ccaaactcac aaggagacat caacctctag acagggaaac      60
agcttcagga tacttccagg agacagagcc accagcagca aaacaaatat tcccatgcct      120
ggagcatggc atagaggaag ctganaaatg tggggctctga ggaagccatt tgagtctggc      180
cactagacat ctccatcagcc acttgtgtga agagatgccc catgacccca gatgcctctc      240
ccacccttac ctccatctca cacacttgag ctttccactc tgtataattc taacatcctg      300
gagaaaaatg gcagtttgac cgaacctgtt cacaacggta gaggctgatt tctaacgaaa      360
cttgtagaat gaagcctgga                                     380

```

```

<210> 161
<211> 114
<212> DNA
<213> Homo sapien

```

```

<400> 161
actccacatc cctctgagc aggcggttgt cgttcaaggt gtatttggcc ttgcctgtca      60
cactgtccac tggccctcta tccacttggg gcttaatccc tcgaaagagc atgt      114

```

```

<210> 162
<211> 177
<212> DNA
<213> Homo sapien

```

```

<400> 162
actttctgaa tcgaatcaaa tgatacttag tgtagtttta atatcctcat atatatcaaa      60
gttttactac tctgataatt ttgtaaaacca ggtaaccaga acatccagtc atacagcttt      120
tggtgatata taacttgcca ataaccagct ctggtgatag ataaaactac tcactgt      177

```

```

<210> 163
<211> 137
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(137)
<223> n = A,T,C or G

```

```

<400> 163
catttataca gacaggcgtg aagacattca cgacaaaaac gcgaaattct atcccgtgac      60
canagaaggc agctacggct actcctacat cctggcgtgg gtggccttcg cctgcacctt      120
catcagcggc atgatgt                                     137

```

```

<210> 164
<211> 469
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(469)
<223> n = A,T,C or G

```

```

<400> 164
cttatcacia tgaatgttct cctgggcagc gttgtgatct ttgccacctt cgtgacttta      60
tgcaatgcat catgctatct catacctaag gagggagttc caggagattc aaccaggaaa      120

```

```

tgcattggatc tcaaaggaaa caaacaccca ataaactcgg agtggcagac tgacaactgt 180
gagacatgca ctgctacga aacagaaatt tcatgttgca cccttgtttc tacacctgtg 240
ggttatgaca aagacaactg ccaaagaatc ttcaagaagg aggactgcaa gtatatcgtg 300
gtggagaaga aggacccaaa aaagacctgt tctgtcagtg aatggataat ctaatgtgct 360
tctagtaggc acagggtccc caggccaggc ctcattctcc tctggcctct aatagtcaat 420
gattgtgtag ccatgcctat cagtataaag atntttgagc aaacacttt 469

```

&lt;210&gt; 165

&lt;211&gt; 195

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(195)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 165

```

acagtttttt atanatatcg acattgccgg cacttggtgtt cagtttcata aagctgggtg 60
atccgctgtc atccactatt ccttggctag agtaaaaatt attcttatag cccatgtccc 120
tgcaggccgc ccgcccgtag ttctcgttcc agtcgtcttg gcacacaggg tgccaggact 180
tcctctgaga tgagt 195

```

&lt;210&gt; 166

&lt;211&gt; 383

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(383)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 166

```

acatcttagt agtgtggcac atcagggggc catcagggtc acagtcactc atagcctcgc 60
cgaggctcga gtccacacca ccggtgtagg tgtgtcfaat ctggggttg gcgcccacct 120
ttggagaagg gatattgctc acacacatgt ccacaaagcc tgtgaactcg ccaagaatt 180
tttcagagc agcctgagca aggggaggat gttcagcttc agctcctcct tcgtcagggtg 240
gatgccaaac tcgtctangg tccgtgggaa gctggtgtcc acntcaccta caacctgggc 300
gangatctta taaaggagct ccnagataaa ctccacgaaa cttctctggg agctgctagt 360
nggggccttt ttggtgaact ttc 383

```

&lt;210&gt; 167

&lt;211&gt; 247

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(247)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 167

```

acagagccag accttggcca taaatgaanc agagattaag actaaacccc aagtcyanat 60
tggagcagaa actggagcaa gaagtgggcc tggggctgaa gttagagacca agggcactgc 120

```

tatanccata cacagagcca actctcaggc caaggcnatg gttggggcag anccagagac	180
tcaatctgan tccaaagtgg tggctggaac actggtcacg acanaggcag tgactctgac	240
tgangtc	247

<210> 168  
 <211> 273  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(273)  
 <223> n = A,T,C or G

<400> 168	
acttctaagt ttctagaag tggaaggatt gtantcatcc tgaaaaatggg ttactttcaa	60
aatccctcan ccttgttctt cactactgtc tatactgana gtgtcatgtt tccacaaagg	120
gctgacacct gagcctgnat ttctactcat ccctgagaag ccctttccag taggggtggc	180
aattcccaac ttcttgcca caagcttccc aggttttctc ccctggaaaa ctccagcttg	240
agtcccagat acactcatgg gctgccctgg gca	273

<210> 169  
 <211> 431  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(431)  
 <223> n = A,T,C or G

<400> 169	
acagccttgg cttcccaaaa ctccacagtc tcagtgcaga aagatcatct tccagcagtc	60
agctcagacc aggggtcaag gatgtgacat caacagtttc tggtttcaga acagggttcta	120
ctactgtcaa atgaccccc atacttctc aaaggctgtg gtaagttttg cacagggtgag	180
ggcagcagaa aggggggtant tactgatgga caccatcttc tctgtatact ccacactgac	240
cttgccatgg gcaaaagccc ctaccacaaa aacaatagga tcaactgttg gcaccagctc	300
acgcacatca ctgacaaccg ggatggaaaa agaantgcc aacttcatac atccaactgg	360
aaagtgatct gatactggat tcttaattac cttcaaaagc ttctgggggc catcagctgc	420
tcgaacactg a	431

<210> 170  
 <211> 266  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(266)  
 <223> n = A,T,C or G

<400> 170	
acctgtgggc tgggctgtta tgcctgtgcc ggctgctgaa agggagttca gaggtggagc	60
tcaaggagct ctgcaggcat ttgccaanc ctctccanag canagggagc aacctacact	120
ccccgctaga aagacaccag attggagctc tgggaggggg agtgggggtg ggcatttgat	180

gtatacttgt cacctgaatg aangagccag agaggaanga gacgaanatg anattggcct 240  
tcaaagctag gggctctggca ggtgga 266

<210> 171

<211> 1248

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (1248)

<223> n = A,T,C or G

<400> 171

```

ggcagccaaa tcataaacgg cgaggactgc agcccgcaact cgcagccctg gcaggcggca      60
ctggtcatgg aaaacgaatt gttctgctcg gccgtcctcg tgcataccga gtgggtgctg      120
tcagccgcac actgtttcca gaagtgaagt gagagctcct acaccatcgg gctgggcctg      180
cacagtcttg aggccgacca agagccaggg agccagatgg tggaggccag cctctccgta      240
cggcaccagg agtacaacag acccttgctc gctaacgacc tcattgctcat caagtgggac      300
gaatccgtgt ccgagtctga caccatccgg agcatcagca ttgcttcgca gtgccctacc      360
gcggggaact cttgcctcgt ttctggctgg ggtctgctgg cgaacggcag aatgcctacc      420
gtgctgcagt gcgtgaacgt gtcggtgggt tctgaggagg tctgcagtaa gctctatgac      480
ccgctgtacc accccagcat gttctgcgcc gccggagggc aagaccagaa ggactcctgc      540
aacggtgact ctggggggcc cctgatctgc aacgggtact tgcagggcct tgtgtctttc      600
ggaaaagccc cgtgtggcca agtggcgctg ccagggtgct acaccaacct ctgcaaatc      660
actgagtggg tagagaaaac cgtccaggcc agttaactct ggggactggg aacctatgaa      720
attgaccccc aaatacatcc tgcggaagga attcaggaat atctgttccc agccccctct      780
ccctcaggcc caggagtcca ggcgccagc cctcctctcc tcaaaccaag ggtacagatc      840
cccagccctc cctccctcag acccaggagt ccagaccccc cagccccctc tcctcagac      900
ccaggagtcc agccccctct cctcagacc caggagtcca gacccccag cccctctctc      960
ctcagaccca ggggtccagg cccccaaccc ctctcctc agactcagag gtccaagccc      1020
ccaaccntc attccccaga cccagaggtc cagggtcccag cccctctctc ctcagaccca      1080
gcggtccaat gccacctaga ctntccctgt acacagtgcc ccttctgtgg acgttgaccc      1140
aaccttacca gttgggtttt cattttngt ccctttcccc tagatccaga aataaagttt      1200
aagagaagng caaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa      1248

```

<210> 172

<211> 159

<212> PRT

<213> Homo sapien

<220>

<221> VARIANT

<222> (1) ... (159)

<223> Xaa = Any Amino Acid

<400> 172

```

Met Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro
  1              5              10              15
Leu Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser
              20              25              30
Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr
              35              40              45
Ala Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly
  50              55              60

```



```

Arg Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu
65              70              75              80
Glu Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe
              85              90              95
Cys Ala Gly Gly Gly Gln Xaa Gln Xaa Asp Ser Cys Asn Gly Asp Ser
              100             105             110
Gly Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe
              115             120             125
Gly Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn
              130             135             140
Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
145              150              155

```

&lt;210&gt; 173

&lt;211&gt; 1265

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (1265)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 173

```

ggcagcccgcc actgcgagcc ctggcaggcg gcaactgggtca tggaaaacga attgttctgc      60
tcggggcgctcc tgggtgcatcc gcagtgggtg ctgtcagccg cacactgttt ccagaactcc      120
tacaccatcg ggctgggcct gcacagtctt gaggccgacc aagagccagg gagccagatg      180
gtggaggcca gcctctccgt acggcaccca gagtacaaca gacccttgct cgctaaccgac      240
ctcatgtctca tcaagtggga cgaatccgtg tccgagtcgt acaccatccg gagcatcagc      300
attgtctcgc agtgccctac cgccggggaac tcttgccctcg tttctggctg gggctctgtg      360
gcgaacgggtg agctcacggg tgtgtgtctg ccctcttcaa ggaggtccctc tgcccagtcg      420
cggggggtgga cccagagctc tgcgtcccag gcagaatgcc taccgtgtcg cagtgcgtga      480
acgtgtcggt ggtgtctgag gagggtctga gtaagctcta tgaccgcgtg taccacccca      540
gcatgttctg cgccggcgga gggcaagacc agaaggactc ctgcaacggt gactctgggg      600
ggccctgat ctgcaacggg tacttgagg gccttgtgtc tttcggaaaa gcccctgtg      660
gccaaagtgg cgtgccaggt gtctacacca acctctgcaa attcactgag tggatagaga      720
aaaccgtcca ggccagttaa ctctggggac tgggaaccca tgaaattgac ccccaaatac      780
atcctgcgga aggaattcag gaatatctgt tcccagcccc tcctccctca ggcccaggag      840
tccaggcccc cagcccctcc tcctcaaac caagggtaca gatccccagc ccctcctccc      900
tcagaccagc gagtccagac ccccagcccc ctctccctc agaccagga gtccagcccc      960
tcctccntca gaccagggag tccagacccc ccagcccctc ctccctcaga cccaggggtt      1020
gaggccccc acccctctc ctccagagtc agaggtccaa gcccaccaac cctcgctccc      1080
cagaccagga ggttnnaggt ccagcccctc ttcctcaga cccagnggtc caatgccacc      1140
tagattttcc ctgnacacag tgccccttg tggnangttg acccaacctt accagttggt      1200
ttttcatttt tngtcccttt cccctagatc cagaaataaa gtttaagaga nngcagaaaa      1265
aaaaa

```

&lt;210&gt; 174

&lt;211&gt; 1459

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (1459)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 174

ggtagccgc	acactgtttc	cagaagtgc	tgacagctc	ctacaccatc	gggtcgggcc	60
tgacagctc	tgagggccgac	caagagccag	ggagccagat	ggtggaggcc	agcctctccg	120
tacggcacc	agagtacaac	agacccttgc	tcgctaacga	cctcatgtct	atcaagttag	180
acgaatccg	gtccgagctc	gacaccatcc	ggagcatcag	cattgtctcg	cagtgcccta	240
ccgcggggaa	ctcttgccctc	gtttctggct	gggtctgct	ggcgaacggt	gagctcacgg	300
gtgtgtgtc	gccctcttca	aggaggtcct	ctgcccagtc	gcgggggctg	acccagagct	360
ctgctccca	ggcagaatgc	ctaccgtgct	gcagtgcgtg	aacgtgtcgg	tggtgtctga	420
ngaggtctgc	antaagctct	atgaccgcct	gtaccacccc	ancatgttct	gcgccggcgg	480
agggaagag	cagaaggact	cctgcaacgt	gagagagggg	aaaggggagg	gcaggcgact	540
caggggaagg	tggaagaagg	ggagacagag	acacacaggg	ccgcatggcg	agatgcagag	600
atggagagac	acacagggag	acagtgcaca	ctagagagag	aaactgagag	aaacagagaa	660
ataaacacag	gaataaagag	aagcaaaagg	agagagaaac	agaaacagac	atggggaggc	720
agaaacacac	acacatagaa	atgcagttga	ccttccaaca	gcattggggc	tgagggcggt	780
gacctccacc	caatagaaaa	tcctcttata	acttttgact	ccccaaaaac	ctgactagaa	840
atagcctact	gttgacgggg	agccttacca	ataacataaa	tagtcgattt	atgcatacgt	900
tttatgcatt	catgatatac	ctttgttgga	attttttgat	atttctaagc	tacacagttc	960
gtctgtgaat	ttttttaa	tgttgcaact	ctcctaaaa	ttttctgatg	tggtttattga	1020
aaaaatccaa	gtataagtgg	acttgtgcat	tcaaacagg	gttgttcaag	ggtcaactgt	1080
gtaccagag	ggaacacagt	acacagattc	atagaggtga	aacacgaaga	gaaacaggaa	1140
aatcaagac	tctacaaaga	ggctgggcag	ggtggctcat	gcctgtaatc	ccagcacttt	1200
gggagggcag	gcaggcagat	cacttgaggt	aaggagttca	agaccagctc	ggccaaaatg	1260
gtgaaatcct	gtctgtacta	aaaatacaaa	agttagctgg	atatgggtgc	aggcgctctg	1320
aatcccgact	acttgggagg	ctgaggcagg	agaattgctt	gaatatggga	ggcagaggtt	1380
gaagtgaagt	gagatcacac	cactatactc	cagctggggc	aacagagtaa	gactctgtct	1440
caaaaaaaaa	aaaaaaaaaa					1459

&lt;210&gt; 175

&lt;211&gt; 1167

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(1167)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 175

gcgcagccct	ggcaggcgcc	actggctcatg	gaaaacgaat	tggtctgtct	gggcgtctctg	60
gtgcatccgc	agtgggtgct	gtcagccgca	cactgttttc	agaactccta	caccatcggt	120
ctgggctcgc	acagtcttga	ggccgaccaa	gagccaggga	gccagatggt	ggaggccagc	180
ctctccgtac	ggcaccaga	gtacaacaga	ctctgtctcg	ctaacgacct	catgctcacc	240
aaagtggagc	aatccgtgct	cgagctgac	accatccgga	gcatacagat	tgcttcgcag	300
tgccctaccg	cggggaactc	ttgcctcgtn	tctggctggg	gtctgctggc	gaacggcaga	360
atgectaccg	tgctgcactg	cgtgaacgtg	tcggtggtgt	ctgaggangt	ctgcagttaag	420
ctctatgacc	cgctgtacca	ccccagcatg	ttctgcgccg	gcggagggga	agaccagaag	480
gactcctgca	acggtgactc	tgggggggccc	ctgatctgca	acgggtactt	gcaggggcctt	540
gtgtctttcg	gaaaagcccc	gtgtggccaa	cttggcgtgc	caggtgtcta	caccaacctc	600
tgcaaatcca	ctgagtggat	agagaaaacc	gtccagncca	gttaactctg	gggactggga	660
acccatgaaa	ttgaccccc	aatacatcct	gcggaangaa	ttcaggaaata	tctgttccca	720
gccccctctc	cctcaggccc	aggagtccag	gccccagcc	cctcctcctc	caaaccaagg	780
gtacagatcc	ccagccccctc	ctccccaga	cccaggagtc	cagaccccc	agccccctnt	840
ccntcagacc	caggagtcca	gccccctctc	cntcagacgc	aggagtccag	acccccagc	900

```

ccntctctcg tcagaccagc ggggtgcaggc ccccaacccc tcttctctca ggtcagagg      960
tccaagcccc caaccctcg ttccccagac ccagaggtnc aggtcccagc cctctctccc      1020
tcagaccagc cgggtccaatg ccacctagan tntccctgta cacagtgcgc ccttggtggca      1080
ngttgaccca accttaccag ttgggttttc attttttgtc cctttcccct agatccagaa      1140
ataaagtnta agagaagcgc aaaaaaa      1167

```

<210> 176  
 <211> 205  
 <212> PRT  
 <213> Homo sapien

<220>  
 <221> VARIANT  
 <222> (1)...(205)  
 <223> Xaa = Any Amino Acid

```

<400> 176
Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp
  1          5          10          15
Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu
  20          25          30
Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val
  35          40          45
Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Leu Leu Leu
  50          55          60
Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser
  65          70          75          80
Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly
  85          90          95
Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met
  100         105         110
Pro Thr Val Leu His Cys Val Asn Val Ser Val Val Ser Glu Xaa Val
  115         120         125
Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala
  130         135         140
Gly Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly
  145         150         155         160
Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys
  165         170         175
Ala Pro Cys Gly Gln Leu Gly Val Pro Gly Val Tyr Thr Asn Leu Cys
  180         185         190
Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Xaa Ser
  195         200         205

```

<210> 177  
 <211> 1119  
 <212> DNA  
 <213> Homo sapien

```

<400> 177
gcgcaactgc agccctggca ggcggcactg gtcattgaaa acgaattgtt ctgctcgggc      60
gtcctgggtg atccgcagt ggtgctgtca gccgcacact gttccagaa ctctacacc      120
atcgggcttg gctgcacag tcttgaggcc gaccaagagc caggagacca gatggtagg      180
gccagcctct ccgtacggca ccagagtagc aacagaccct tgctcgctaa cgacctcatg      240
ctcatcaagt tggacgaatc cgtgtccgag tctgacacca tccggagcat cagcattgct      300

```

```

tcgcagtgcc ctaccgcggg gaactcttgc ctcgtttctg gctgggggtct gctggcgaaac 360
gatgctgtga ttgccatcca gtcccagact gtgggaggct gggagtgtga gaagctttcc 420
caaccctggc aggggtgtac catttcggca acttccagtg caaggacgtc ctgctgcatc 480
ctcactgggt gctcactact gctcactgca tcacccgga cactgtgac aactagccag 540
caccatagtt ctccgaagtc agactatcat gattactgtg ttgactgtgc tgtctattgt 600
actaaccatg ccgatgttta ggtgaaatta gcgtcacttg gcctcaacca tcttggtatc 660
cagttatcct cactgaattg agatttcctg ctccagtgtc agccattccc acataatttc 720
tgacctacag aggtgagggg tcatatagct cttcaaggat gctgggtactc ccctcacaaa 780
ttcattttct ctgttgtagt gaaaggtgcg cctctggag cctcccaggg tgggtgtgca 840
ggtcacaatg atgaatgtat gatcgtgttc ccattacca aagcctttaa atccctcatg 900
ctcagtagac cagggcaggt ctagcatttc ttcatttagt gtatgctgtc cattcatgca 960
accacctcag gactcctgga ttctctgcct agttgagctc ctgcatgctg cctccttggg 1020
gaggtgaggg agagggccca tggttcaatg ggatctgtgc agttgtaaca cattaggtgc 1080
ttaataaaca gaagctgtga tgttaaaaaa aaaaaaaaa 1119

```

&lt;210&gt; 178

&lt;211&gt; 164

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(164)

&lt;223&gt; Xaa = Any Amino Acid

&lt;400&gt; 178

```

Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp
 1          5          10          15
Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu
 20          25          30
Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val
 35          40          45
Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu
 50          55          60
Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser
 65          70          75          80
Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly
 85          90          95
Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Asp Ala Val
100          105          110
Ile Ala Ile Gln Ser Xaa Thr Val Gly Gly Trp Glu Cys Glu Lys Leu
115          120          125
Ser Gln Pro Trp Gln Gly Cys Thr Ile Ser Ala Thr Ser Ser Ala Arg
130          135          140
Thr Ser Cys Cys Ile Leu Thr Gly Cys Ser Leu Leu Leu Thr Ala Ser
145          150          155          160
Pro Gly Thr Leu

```

&lt;210&gt; 179

&lt;211&gt; 250

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 179

ctggagtgcc	tgtgtgtttc	aagccccctgc	aggaagcaga	atgcaccttc	tgaggcacct	60
ccagctgccc	ccggccgggg	gatcgaggc	tcggagcacc	cttgcccggc	tgtgattgct	120
gccaggcact	gttcatctca	gcttttctgt	ccctttgctc	ccggcaagcg	cttctgctga	180
aagttcatat	ctggagcctg	atgtcttaac	gaataaagg	cccatgctcc	acccgaaaaa	240
aaaaaaaaa						250

<210> 180  
 <211> 202  
 <212> DNA  
 <213> Homo sapien

<400> 180						
actagtccag	tgtggtggaa	ttccattgtg	ttgggcccga	cacaatggct	acctttaaca	60
tcacccagac	ccgcccctg	cccggtcccc	acgtgctgc	taacgacagt	atgatgctta	120
ctctgctact	cggaaactat	ttttatgtaa	ttaatgtatg	ctttcttggt	tataaatgcc	180
tgatttaaaa	aaaaaaaaa	aa				202

<210> 181  
 <211> 558  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (558)  
 <223> n = A,T,C or G

<400> 181						
tcctyttgkt	naggtttkkg	agacamccck	agacctwaan	ctgtgtcaca	gacttcyngg	60
aatgtttagg	cagtgctagt	aatttcytcg	taatgattct	gttataactt	tcctnattct	120
ttattcctct	ttcttctgaa	gattaatgaa	gttgaaaatt	gaggtggata	aatacaaaaa	180
ggtagtgtga	tagtataagt	atctaagtcg	agatgaaagt	gtgttatata	tatccattca	240
aaattatgca	agtttagtaat	tactcaggg	taactaaatt	actttaatat	gctgttgaac	300
ctactctgtt	ccttggtctg	aaaaaattat	aaacaggact	ttgttagttt	gggaagccaa	360
attgataata	ttctatgttc	taaaagttgg	gctatacata	aattattaag	aaatatggaw	420
ttttattccc	aggaatatgg	kgttcatttt	atgaatatta	cscrggatag	awgtwtgagt	480
aaaaycagtt	ttggtwaata	ygtwaatatg	tcmtaaataa	acaakgcttt	gacttatttc	540
caaaaaaaaa	aaaaaaaaa					558

<210> 182  
 <211> 479  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (479)  
 <223> n = A,T,C or G

<400> 182						
acagggwttk	grggatgcta	agscgccrga	rwtyggttga	tccaaccctg	gcttwttttc	60
agaggggaaa	atggggcccta	gaagttacag	mecatytagy	tgggtcgmtg	gcacccctgg	120
cstcacacag	astccccagt	agctgggact	acaggcacac	agtcactgaa	gcaggccctg	180
ttwgcaattc	acgttgccac	ctccaaacta	aacattcttc	atatgtgatg	tccttagtca	240
ctaaggttaa	actttcccac	ccagaaaagg	caacttagat	aaaactcttag	agtactttca	300

tactmttcta	agtcctcttc	cagcctcact	kkgagtcctm	cytggggggt	gataggaant	360
ntctcttggc	tttctcaata	aartctctat	ycatctcatg	tttaatttgg	tacgcataara	420
awtgstgara	aaattaaaaa	gttctgggty	macctttaaaa	aaaaaaaaaa	aaaaaaaaaa	479

<210> 183  
 <211> 384  
 <212> DNA  
 <213> Homo sapien

<400> 183						
aggcgggagc	agaagctaaa	gccaaagccc	aagaagagtg	gcagtgccag	caactgggtgcc	60
agtaccagta	ccaataacag	tgccagtgcc	agtgccagca	ccagtggtgg	cttcagtgct	120
ggtgccagcc	tgaccgccc	tctcacattt	gggctcttcg	ctggccttgg	tggagctggg	180
gccagcacca	gtggcagctc	tggtgcctgt	ggtttctcct	acaagtgaga	ttttagatat	240
tgtaatcct	gccagtcctt	ctcttcaagc	cagggtgcat	cctcagaaac	ctactcaaca	300
cagcactcta	ggcagccact	atcaatcaat	tgaagttgac	actctgcatt	aratctattt	360
gccatttcaa	aaaaaaaaaa	aaaa				384

<210> 184  
 <211> 496  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (496)  
 <223> n = A, T, C or G

<400> 184						
accgaattgg	gaccgctggc	ttataagcga	tcattgtynt	ccrgtatcac	ctcaacgagc	60
agggagatcg	agtcctatac	ctgaagaaat	ttgacccgat	gggacaacag	acctgctcag	120
cccattctgc	tcggttctcc	ccagatgaca	aatactctsg	acaccgaatc	accatcaaga	180
aacgcttcaa	ggtgctcatg	accagcaaac	cgcgccctgt	cctctgaggg	tcctttaaac	240
tgatgtcttt	tctgccacct	gttacccttc	ggagactccg	taaccaaac	cttcggactg	300
tgagccctga	tgctcttttg	ccagccatac	tctttggcat	ccagtctctc	gtggcgattg	360
attatgcttg	tgtgaggcaa	tcattggtggc	atcaccata	aagggaaac	atttgacttt	420
tttttctcat	atttttaatt	actacmagaw	tattwmagaw	waaatgawtt	gaaaaactst	480
taaaaaaaaa	aaaaaa					496

<210> 185  
 <211> 384  
 <212> DNA  
 <213> Homo sapien

<400> 185						
gctggtagcc	tatggcgkkg	cccacggagg	ggctcctgag	gccacggrac	agtgacttcc	60
caagtatcyt	gcgscgcgtc	ttctaccgtc	cctacctgca	gatcttcggg	cagattcccc	120
aggaggacat	ggagctggcc	ctcatggagc	acagcaactg	ytcttcggag	cccggtctct	180
gggcacaccc	tcttggggcc	caggcgggca	cctgcgtctc	ccagtatgcc	aactggcttg	240
tggtgctgct	ctctgcctac	ttcctgctcg	tgcccaacat	cctgctggtc	aacttgctca	300
ttgccatggt	cagttacaca	ttcgccaaag	tacaggggcaa	cagcgatctc	tactgggaag	360
gcgcagcgtt	accgcctcat	ccgg				384

<210> 186  
 <211> 577

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(577)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 186

gagttagctc	ctccacaacc	ttgatgaggt	cgtctgcagt	ggcctctcgc	ttcataccgc	60
tnccatcgtc	atactgtagg	tttgccacca	cytcttgga	tcttggggcg	gcntaatatt	120
ccaggaaact	ctcaatcaag	tcaccgtcga	tgaaacctgt	gggctgggtc	tgctctccgc	180
tcggtgtgaa	aggatctccc	agaaggagtg	ctcgatcttc	cccacacttt	tgatgacttt	240
attgagtcga	ttctgcattg	ccagcaggag	gttgtagacc	ctctctgaca	gtgaggtcac	300
cagccctatc	atgccgttga	mcgtgccgaa	garcaccgag	ccttgtgtgg	gggkkgaa	360
ctcaccacga	ttctgcatta	ccagagagcc	gtggcaaaa	acattgacaa	actcgcccag	420
gtggaaaaag	amcamctcct	ggargtgctn	gccgctcttc	gtcmgttggt	ggcagcgctw	480
tccttttgac	acacaaaaca	gttaaaggca	ttttcagccc	ccagaaantt	gtcatcatcc	540
aagatntcgc	acagcactna	tccagtggg	attaaat			577

&lt;210&gt; 187

&lt;211&gt; 534

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(534)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 187

aacatcttcc	tgtataatgc	tgtgtaatat	cgatccgatn	ttgtctgstg	agaatycatw	60
actkggaaaa	gmaacattaa	agcctggaca	ctggatttaa	aattcacaat	atgcaacact	120
ttaaacagtg	tgtcaatctg	ctcccyynac	ttgtcatca	ccagctctgg	aakaagggtg	180
tgccctatcc	acacctgtta	aaaggcgct	aagcattttt	gattcaacat	cttttttttt	240
gacacaagtc	cgaaaaaagc	aaaagtaaac	agttatyaat	ttgttagcca	attcactttc	300
ttcatgggac	agagccatyt	gatttaaaaa	gcaaattgca	taatattgag	cttygggagc	360
tgatatttga	gcggaagagt	agcctttcta	cttcaccaga	cacaactccc	tttcatattg	420
ggatgttnac	naaagtwatg	tctctwacag	atgggatgct	tttggggcaa	ttctgttctg	480
aggatctccc	agtttattta	ccacttgac	aagaaggcgt	tttcttcttc	agge	534

&lt;210&gt; 188

&lt;211&gt; 761

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(761)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 188

agaaaccagt	atctctnaaa	acaacctctc	ataccttggt	gacctaat	ttgtgtgcgtg	60
tggtgtgtgc	cgcatattat	atagacaggc	acatcttttt	tacttttgtta	aaagcttatg	120
cctcttttgt	atctatatct	gtgaaagttt	taatgatctg	ccataatgtc	ttggggacct	180

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ttgtcttctg tgtaaatggt actagagaaa acacctatnt tatgagtcac tctagttngt 240
tttattcgac atgaaggaaa ttccagatn acaacactna caaactctcc ctkgackarg 300
ggggacaaaag aaaagcaaaa ctgamcataa raacaaatwa cctggtgaga arttgcataa 360
acagaaatwr ggtagtatat tgaarnacag catcattaaa rmgttwkttt wttctccctt 420
gcaaaaaaca tgtacngact tcccgttgag taatgccaaag ttgttttttt tatnatataa 480
cttgcccttc attacatggt tnaaagtggg gtggtggggc aaaatattga aatgatggaa 540
ctgactgata aagctgtaca aataagcagt gtgcctaaca agcaacacag taatgttgac 600
atgcttaatt cacaatgctt aatttcatta taaatgtttg ctaaaatata ctttgaacta 660
tttttctgtn ttcccagagc tgagatntta gattttatgt agtatnaagt gaaaaantac 720
gaaataataa acattgaaga aaaaananaa aanaaaaaaa a 761

```

```

<210> 189
<211> 482
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(482)
<223> n = A,T,C or G

```

```

<400> 189
tttttttttt ttgtccgatn ctactatttt attgcaggan gtgggggtgt atgcaccgca 60
caccgggggt atnagaagca agaagggaagg agggagggca cagccccttg ctgagcaaca 120
aagccgcctg ctgctctctc tgtctgtctc ctggtgcagg cacatgggga gaccttcccc 180
aaggcagggg ccaccagtcg aggggtggga atacaggggg tgggngtgt gcataagaag 240
tgataggcac aggccacccg gtacagaccc ctgcgctcct gacaggtnga ttctgaccag 300
gtcattgtgc cctgccaggc cacagcgtna atctggaaaa gacagaatgc ttctcttttc 360
aatattggct ngctcatngaa ngggcatttt tccaanttng gctnngtctt ggtacncttg 420
gttcggccca gctcncgctc caaaaantat tcacccnnct ccnaattgct tgcnggnccc 480
cc

```

```

<210> 190
<211> 471
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(471)
<223> n = A,T,C or G

```

```

<400> 190
tttttttttt ttttaaaaca gtttttcaca aaaaaattta ttagaagaat agtggttttg 60
aaaactctcg catccagtga gaactaccat acaccacatt acagctngga atgtnctcca 120
aatgtctggt caaatgatac aatggaaacca ttcaatctta cacatgcacg aaagaacaag 180
cgcttttgac atacaatgca caaaaaaaa aggggggggg gaccacatgg attaaaattt 240
taagtactca tcacatacat taagacacag ttctagtcca gtcnaaaatc agaactgent 300
tgaaaaattt catgtatgca atccaaccaa agaacttnat tgggtgatcat gantnctcta 360
ctacatcnac cttgatcatt gccaggaaac aaaagttnaa ancacnngt acaaaaanaa 420
tctgtaattn anttcaacct ccgtacngaa aaatnttntt tatacactcc c 471

```

```

<210> 191
<211> 402
<212> DNA

```



<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (402)

<223> n = A,T,C or G

<400> 191

gagggattga aggtctgttc tastgtcggm ctgttcagcc accaactcta acaagttgct	60
gtcttccact cactgtctgt aagcttttta acccagacwg tatcttcata aatagaacaa	120
attcttcacc agtcacatct tctaggacct ttttggattc agttagtata agctcttcca	180
cttctcttgt taagacttca tctggtaaag tcttaagttt tgtagaaagg aattyaattg	240
ctcgttctct aacaatgtcc tctccttgaa gtatttggtc gaacaaccca cctaaagtcc	300
ctttgtgcat ccattttaaa tatacttaat agggcattgk tncactaggt taaattctgc	360
aagagtcatc tgtctgcaaa agttgcgtta gtatatctgc ca	402

<210> 192

<211> 601

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (601)

<223> n = A,T,C or G

<400> 192

gagctcggat ccaataatct ttgtctgagg gcagcacaca tatncagtgc catggnaact	60
ggtctacccc acatgggagc agcatgccgt agntatataa ggtcattccc tgagtcagac	120
atgcyytttt gaytaccgtg tgccaagtgc tgggtattct yaacacacyt ccatcccyt	180
cttttctgga aaaactggca cttktctgga actagcarga catcacttac aaattcacc	240
acgagacact tgaagggtgt aacaaagcga ytcttgcatt gctttttgtc cctccggcac	300
cagttgtcaa tactaaccgc ctgggttgcc tccatcacat ttgtgatctg tagctctgga	360
tacatctcct gacagtactg aagaacttct tcttttgttt caaaagcacc tcttgggtgc	420
tgttggatca ggttccatt tcccagtcyg aatgttcaca tggcatattt wactccac	480
aaaacattgc gatttgaggc tcagcaacag caaatcctgt tccggcattg gctgcaagag	540
cctcgatgta gccggccagc gccaaaggag gcgccgtgag cccaccacgc agcagaagca	600
g	601

<210> 193

<211> 608

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (608)

<223> n = A,T,C or G

<400> 193

atacagccca natcccacca cgaagatgag cttgttgact gagaacctga tgcggtcact	60
ggtcccgtg tagccccagc gactctccac ctgctggaag cggttgatgc tgcactcytt	120
cccacgcag gcagmagcgg gscgggtcaa tgaactccay tcgtggcttg gggtkgacgg	180
tkaagtgcag gaagaggctg accacctcgc ggtccaccag gatgcccgac tgtgcgggac	240
ctgcagcgaa actcctcgat ggtcatgagc gggaaagcgaa tgaggccacg ggccttgccc	300

```

agaaccttcc gacctgttctc tggcgctcacc tgcagctgct gccgctgaca ctccggcctcg      360
gaccagcgga caaacgcgrrt tgaacagccg caccctcacgg atgcccagtg tgtcgcgctc      420
caggammgsc accagcgtgt ccagggtcaat gtcggtgaag ccctccgcgg gtratggcgt      480
ctgcagtggt tttgtcgatg ttctccaggc acaggctggc cagctgcggg tcactgaaga      540
gtcgcgcctg cgtgagcagc atgaaggcgt tgtcggctcg cagttcttct tcaggaactc      600
cacgcaat                                     608

```

```

<210> 194
<211> 392
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(392)
<223> n = A,T,C or G

```

```

<400> 194
gaacggctgg acctgtccctc gcattgtgct tgctggcagg gaataccttg gcaagcagyt      60
ccagtccgag cagcccccaga ccgctgccgc ccgaagctaa gcctgcctct ggccttcccc      120
tccgcctcaa tgcagaacca gtatggggag cactgtgttt agagttaaga gtgaacactg      180
tttgatttta cttgggaatt tcctctgtta tatagctttt cccaatgcta atttccaaac      240
aacaacaaca aaataacatg tttgcctggt aagttgtata aaagttagtg attctgtatt      300
taaagaaat attactgtta catatactgc ttgcaatttc tgtatttatt gktnctstgg      360
aaataaatat agttattaaa ggtgtgcant cc                                     392

```

```

<210> 195
<211> 502
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(502)
<223> n = A,T,C or G

```

```

<400> 195
ccsttkgagg ggtkaggkyc cagtttyccga gtggaagaaa caggccagga gaagtgcgtg      60
ccgagctgag gcagatgttc ccacagtgac cccagagacc stgggstata gtytctgacc      120
cctcncaagg aaagaccacs ttctggggag atgggctgga gggcaggacc tagaggcacc      180
aagggaaagg cccattccgg ggstgttccc cgaggaggaa gggaaagggc tctgtgtgcc      240
ccccasgagg aagaggccct gagtcctggg atcagacacc ccttcacgtg tatccccaca      300
caaatgcaag ctaccaaagg tcccccttca gtccccctcc stacaccctg amcgggccact      360
gscscacacc caccagagc acgccaccgc ccatggggar tgtgctcaag gartcgcnng      420
gcarcgtgga catctngtcc cagaaggggg cagaatctcc aatagangga ctgarcmstt      480
gctnanaaaa aaaaaaaaaa aa                                     502

```

```

<210> 196
<211> 665
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(665)

```

<223> n = A,T,C or G

```

<400> 196
ggttacttgg tttcattgcc accacttagt ggaatgcatt tagaaccatt ttgtctgctc      60
cctctggaag ccttgcgcag agcggacttt gtaattggtg gagaataact gctgaatttt      120
wagctgtttk gagttgatts gcaccactgc acccacaact tcaatatgaa aacyawttga      180
actwatttat tatcttgatg aaagtataac aatgaaaatt ttgttcatac tgtattkac      240
aagtatgatg aaaagcaawa gatatatatt cttttattat gttaaattat gattgccatt      300
attaatcggc aaaatgtgga gtgtatgttc ttttcacagt aatatatgcc ttttgtaact      360
tcacttgggt attttattgt aaatgattta caaaattcct aatttaagar aatggatgt      420
wataatttat tcattaattt ctttctkgt ttacgtwaat ttgaaaaga wtgcattgatt      480
tcttgacaga aatcgatcct gatgctgtgg aagtagtttg acccacatcc ctatgagttt      540
ttcttagaat gtataaagg ttagtccccat cnaacttcaa agaaaaaaat gaccacatac      600
tttgcataca ggctgaaatg tggcatgctn ttctaattcc aactttataa actagcaaan      665
aagt

```

<210> 197

<211> 492

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(492)

<223> n = A,T,C or G

```

<400> 197
ttttnttttt ttttttttgc aggaaggatt ccatttattg tggatgcatt ttcacaatat      60
atgtttattg gagcgatcca ttatcagtga aaagtatcaa gtgtttataa natttttagg      120
aaggcgagatt cacagaacat gctngtcngc ttgcagtttt acctcgtna gatnacagag      180
aattatagtc naaccagtaa acnaggaatt tacttttcaa aagattaaat ccaaactgaa      240
caaaattcta ccttgaaact tactccatcc aaatatgtga ataanagta gcagtgtac      300
attctcttct gaactttaga ttttctagaa aaatatgtaa tagtgatcag gaagagctct      360
tgttcaaaag tacaacnaag caatgttccc ttaccatagg ccttaattca aactttgatc      420
catttcactc ccatacggg agtcaatgct acctgggaca cttgtatttt gtctatnctg      480
ancntggctt aa

```

<210> 198

<211> 478

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(478)

<223> n = A,T,C or G

```

<400> 198
tttnttttgn atttcantct gtannaanta ttttcattat gtttattana aaaatatnaa      60
tgtntccacn acaaatcatn ttacntnagt aagaggccan ctacattgta caacatacac      120
tgagtatatt tgaaaaagga caagttttaa gtanacncat attgccganc atancacatt      180
tatacatggc ttgattgata tttagcacag canaaactga gtgagttacc agaaaanaa      240
natatatgtc aatcngattt aagatacaaa acagatccta tggtagatan catcntgtag      300
gagttgtggc tttatgttta ctgaaagtca atgcagttcc tgtacaaaga gatggccgta      360
agcattctag taccttactc ccattggttaa gaatcgtaca cttatgttta catatgtnta      420

```

gggtaagaat tgtgttaagt naanttatgg agaggtccan gagaaaaatt tgatncaa 478

<210> 199  
 <211> 482  
 <212> DNA  
 <213> Homo sapien  
  
 <220>  
 <221> misc\_feature  
 <222> (1)...(482)  
 <223> n = A,T,C or G

<400> 199  
 agtgacttgt cctccaacaa aacccttga tcaagtttgt ggcactgaca atcagaccta 60  
 tgctagtcc tgtcatctat tcgtactaa atgcagactg gaggggacca aaaaggggca 120  
 tcaactccag ctggattatt ttggagcctg caaatctatt cctacttgta cggactttga 180  
 agtgattcag ttctctctac ggatgagaga ctggctcaag aatatcctca tgcagcttta 240  
 tgaagcncac tctgaacacg ctggttatct nagatgagaa ncagagaaat aaagtcnaga 300  
 aaatttacct ggangaaaag aggccttngg ctggggacca tcccattgaa ccttctctta 360  
 anggacttta agaanaaaact accacatgtn tgtngtatcc tgggtccngg ccgtttantg 420  
 aacntngacn ncaccttnt ggaatanant cttgacngcn tcctgaactt gtcctctctg 480  
 ga 482

<210> 200  
 <211> 270  
 <212> DNA  
 <213> Homo sapien  
  
 <220>  
 <221> misc\_feature  
 <222> (1)...(270)  
 <223> n = A,T,C or G

<400> 200  
 cggccgcaag tgcaactcca gctggggccg tgcggacgaa gattctgcc a gcagttggtc 60  
 cgactgcgac gacggcgccg gcgacagtcg cagggtgcagc gcgggcgcct ggggtcttgc 120  
 aaggctgagc tgacgcccga gaggtcgtgt cacgtccac gacctgacg ccgtcgggga 180  
 cagccggaac agagcccgt gaangcggga ggcctcgggg agcccctcgg gaagggcgcc 240  
 ccgagagata cgcaggtgca ggtggccgcc 270

<210> 201  
 <211> 419  
 <212> DNA  
 <213> Homo sapien  
  
 <220>  
 <221> misc\_feature  
 <222> (1)...(419)  
 <223> n = A,T,C or G

<400> 201  
 tttttttttt ttttgaatc tactgcgagc acagcaggtc agcaacaagt ttatttttgc 60  
 gctagcaagg taacagggta gggcatgggt acatgttcag gtcaacttcc tttgtcgtgg 120  
 ttgattgggt tgtctttatg ggggcggggg ggggtagggg aaancgaagc anaantaaca 180  
 tggagtgggt gcaccctccc tgtagaacct ggttacnaaa gcttggggca gttcacctgg 240

tctgtgaccg	tcattttctt	gacatcaatg	ttattagaag	tcaggatatac	ttttagagag	300
tcactgtnt	ctggaggag	attaggggtt	cttgccaana	tccaancaa	atccacntga	360
aaaagttaga	tgatncangt	acngaatacc	ganggcatan	tttctcatant	cgggtggcca	419

&lt;210&gt; 202

&lt;211&gt; 509

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(509)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 202

tttntttttt	ttttttttt	ttttttttt	ttttttttt	ttttttttt	ttttttttt	60
tggcacttaa	tccattttta	tttcaaaatg	tctacaaant	ttnaatncnc	cattatacng	120
gtnattttnc	aaaatctaaa	nnttattcaa	atntnagcca	aantccttac	ncaaatnnaa	180
tacnncnaaa	aatcaaaaat	atacntntct	ttcagcaaac	ttngttacat	aaattaaaaa	240
aatatatacg	gctggtgttt	tcaaagtaca	attatcttaa	cactgcaaac	atnttttnaa	300
ggaactaaaa	taaaaaaaa	cactnccgca	aagggttaag	ggaacaacaa	attcntttta	360
caacancnnc	nattataaaa	atcatatctc	aaatcttagg	ggaatatata	cttcacacng	420
ggaatctaac	ttttactnca	ctttgtttat	ttttttanaa	ccattgtntt	gggccaacaa	480
caatggnaat	nccnccnnc	tggactagt				509

&lt;210&gt; 203

&lt;211&gt; 583

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(583)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 203

ttttttttt	tttttttga	ccccctctt	ataaaaaaca	agttaccatt	ttattttact	60
tacacatatt	tattttataa	ttggtattag	atattcaaaa	ggcagctttt	aaaatcaaac	120
taaatggaaa	ctgccttaga	tacataattc	ttaggaatta	gcttaaaatc	tgccataaagt	180
gaaaatcttc	tctagctctt	ttgactgtaa	atttttgact	cttgtaaaac	atccaaattc	240
atttttcttg	tctttaaaat	tatctaattc	ttccattttt	tccttattcc	aagtcaattt	300
gcttctctag	cctcatttcc	tagctcttat	ctactattag	taagtgggctt	ttttcctaaa	360
agggaaaaca	ggaagagana	atggcacaca	aaacaaacat	tttatattca	tattttctacc	420
tacgttaata	aaatagcatt	ttgtgaagcc	agctcaaaag	aagggttaga	tccttttatg	480
tcatttttag	tcactaaacg	atatcnaaag	tgccagaatg	caaaagggtt	gtgaacattt	540
attcaaaagc	taatataga	tatttcacat	actcatcttt	ctg		583

&lt;210&gt; 204

&lt;211&gt; 589

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(589)

<223> n = A,T,C or G

<400> 204

tttttttttt	tttttttttt	tttttttttt	tttttttttt	ttganaatga	ggatcgagtt	60
tttctactctc	tagatagggc	atgaagaaaa	ctcatctttc	cagcttttaa	ataacaatca	120
aatctcttat	gctatatcat	attttaagtt	aaactaatga	gtcactggct	tatcttctcc	180
tgaaggaaat	ctgttcattc	ttctcattca	tatagttata	tcaagtacta	ccttgcatat	240
tgagagggtt	ttcttctcta	tttacacata	tatttccatg	tgaatttgta	tcaaaccctt	300
attttcatgc	aaactagaaa	ataatgtntt	cttttgcata	agagaagaga	acaatatnag	360
cattacaaaa	ctgctcaaat	tggttggttaa	gnttatccat	tataattagt	tnggcaggag	420
ctaatacaaa	tcacatttac	ngacnagcaa	taataaaaact	gaagtaccag	ttaaataatcc	480
aaaataatta	aaggaaacatt	tttagcctgg	gtataattag	ctaattcact	ttacaagcat	540
ttattnagaa	tgaattcaca	tggtattatt	ccntagccca	acacaatgg		589

<210> 205

<211> 545

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(545)

<223> n = A,T,C or G

<400> 205

tttttttttt	ttttttcagt	aataatcaga	acaatattta	tttttatatt	taaaattcat	60
agaaaagtgc	cttacattta	ataaaagttt	gtttctcaa	gtgatcagag	gaattagata	120
tngtcttgaa	caccaatatt	aatttgagga	aaatacacca	aaatacatta	agtaaattat	180
ttaagatcat	agagcttgya	agtgaagaa	taaaatttga	cctcagaaac	tctgagcatt	240
aaaaatccac	tattagcaaa	taaattacta	tggacttctt	gctttaattt	tgtgatgaat	300
atgggggtgc	actgggtaac	caacacattc	tgaaggatac	atcacttagt	gatagattct	360
tatgtacttt	gctanatnac	gtggatatga	gttgacaagt	ttctctttct	tcaatctttt	420
aaggggcnga	ngaagttagg	aagaaaagaa	aaggattacg	catactgttc	tttctatngg	480
aaggattaga	tatgtttcct	ttggccaatat	taaaaaaata	ataatgttta	ctactagtga	540
aacc						545

<210> 206

<211> 487

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(487)

<223> n = A,T,C or G

<400> 206

tttttttttt	tttttttagc	aagtttctna	tttttattat	aattaaagtc	ttggtcattt	60
catttattag	ctctgcaact	tacatattta	aattaaagaa	acgttnttag	acaactgtna	120
caatttataa	atgtaagggtg	ccattattga	gtanatata	tcctccaaga	gtggatgtgt	180
cccttctccc	accaactaat	gaancagcaa	cattagttta	attttattag	tagatnatac	240
actgtctcaa	acgctaattc	tcttctccat	ccccatgtng	atattgtgta	tatgtgtgag	300
ttggttnagaa	tgcatcanca	atctnacaat	caacagcaag	atgaagctag	gcntgggctt	360
tcgggtgaaaa	tagactgtgt	ctgtctgaat	caaatgatct	gacctatcct	cggtggcaag	420
aactcttcga	accgcttctc	caaaggcngc	tgccacattt	gtggcncctn	ttgcacttgt	480

ttcaaaa

487

<210> 207  
<211> 332  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(332)  
<223> n = A,T,C or G

<400> 207  
tgaattggct aaaagactgc atttttanaa ctagcaactc ttattttcttt cctttaaaaa 60  
tacatagcat taaatcccaa atcctattta aagacctgac agcttgagaa ggtcactact 120  
gcattttatag gaccttctgg tggttctgct gttacntttg aantctgaca atccttgana 180  
atctttgcat gcagaggagg taaaagggtat tggattttca cagaggaana acacagcgca 240  
gaaatgaagg ggccaaggctt actgagcttg tccactggag ggctcatggg tgggacatgg 300  
aaaagaaggc agcctaggcc ctggggagcc ca 332

<210> 208  
<211> 524  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(524)  
<223> n = A,T,C or G

<400> 208  
agggcggtgt gcggagggcg ttactgtttt gtctcagtaa caataaatat aaaaagactg 60  
gttggtgtcc ggcccatcc aaccacgaag ttgattttct ttgtgtgcag agtgactgat 120  
tttaaaggac atggagcttg tcacaatgac acaatgtcac agtgtgaagg gcacactcac 180  
tcccgcgtga ttacacattta gcaaccaaca atagctcatg agtccatact tgtaaatatc 240  
tttggcagaa tactttttga aacttgcaga tgataactaa gatccaagat atttcccaaa 300  
gtaaatagaa gtgggtcata atattaatta cctgttcaca tcagcttcca tttaacaagtc 360  
atgagcccg acactgacat caaactaagc ccacttagac tcctcaccac cagtctgtcc 420  
tgtcatcaga caggaggctg tcaccttgac caaattctca ccagtcacac atctatccaa 480  
aaaccattac ctgatccact tccggtaatg caccaccttg gtga 524

<210> 209  
<211> 159  
<212> DNA  
<213> Homo sapien

<400> 209  
gggtgaggaa atccagagtt gccatggaga aaattccagt gtcagcattc ttgctccttg 60  
tggccctctc ctacactctg gccagagata ccacagtcaa acctggagcc aaaaaggaca 120  
caaaggatc tcgacccaaa ctgcccaga ccctctcca 159

<210> 210  
<211> 256  
<212> DNA  
<213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(256)  
 <223> n = A,T,C or G

<400> 210  
 actccctggc agacaaaggc agaggagaga gctctgttag ttctgtgttg ttgaactgcc 60  
 actgaatttc ttccacttg gactattaca tgccantga gggactaatg gaaaaacgta 120  
 tggggagatt ttanccaatt tangtntgta aatggggaga ctggggcagg cgggagagat 180  
 ttgcaggggtg naaatgggan ggctgggttg ttanatgaac agggacatag gaggtaggca 240  
 ccaggatgct aaatca 256

<210> 211  
 <211> 264  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(264)  
 <223> n = A,T,C or G

<400> 211  
 acattgtttt ttgagataa agcattgaga gagctctcct taacgtgaca caatggaagg 60  
 actggaacac ataccacat ctttgttctg agggataatt ttctgataaa gtcttgctgt 120  
 atattcaagc acatatgtta tatattattc agttccatgt ttatagccta gttaaggaga 180  
 ggggagatac attcngaaag aggactgaaa gaaatactca agtnggaaaa cagaaaaaga 240  
 aaaaaaggag caaatgagaa gcct 264

<210> 212  
 <211> 328  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(328)  
 <223> n = A,T,C or G

<400> 212  
 acccaaaaat ccaatgctga atatttggtc tcattattcc canattcttt gattgtcaaa 60  
 ggatttaatg ttgtctcagc ttgggcactt cagttaggac ctaaggatgc cagccggcag 120  
 gtttatatat gcagcaacaa tattcaagcg cgacaacagg ttattgaact tgcccgccag 180  
 ttnaatttca ttcccattga cttgggattc ttatcatcag ccagagagat tgaaaattta 240  
 cccctacnac tctttactct ctgganaggg ccagtgggtg tagctataag cttggccaca 300  
 ttttttttct cttttattct ttgtcaga 328

<210> 213  
 <211> 250  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature



&lt;222&gt; (1)...(250)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 213

acttatgagc	agagcgacat	atccnagtgt	agactgaata	aaactgaatt	ctctccagtt	60
taaagcattg	ctcactgaag	ggatagaagt	gactgccagg	agggaaaagta	agccaaggct	120
cattatgcca	aagganatat	acattttcaat	tctccaaact	tcttctcat	tccaagagtt	180
ttcaatattt	gcatgaacct	gctgataanc	catgttaana	aacaaatata	tctctnacct	240
tctcatcggt						250

&lt;210&gt; 214

&lt;211&gt; 444

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(444)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 214

accagaatc	caatgctgaa	tatttggtt	cattattccc	agattctttg	attgtcaaag	60
gatttaagt	tgtctcagct	tgggcacttc	agttaggacc	taaggatgcc	agccggcagg	120
tttatatatg	cagcaacaat	attcaagcgc	gacaacaggt	tattgaactt	gcccggcagt	180
tgaatttcat	tccattgac	ttgggacct	tatcatcagc	canagagatt	gaaaatttac	240
ccctacgact	ctttactctc	tggagagggc	cagtgggtgt	agctataaag	ttggccacat	300
ttttttttcc	tttattcctt	tgtcagagat	gcgattcacc	catatgctan	aaaccaacag	360
agtgactttt	acaaaattcc	tataganatt	gtgaataaaa	ccttacctat	agttgccatt	420
actttgctct	ccctaataata	cctc				444

&lt;210&gt; 215

&lt;211&gt; 366

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(366)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 215

acttatgagc	agagcgacat	atccaagtgt	anactgaata	aaactgaatt	ctctccagtt	60
taaagcattg	ctcactgaag	ggatagaagt	gactgccagg	agggaaaagta	agccaaggct	120
cattatgcca	aagganatat	acattttcaat	tctccaaact	tcttctcat	tccaagagtt	180
ttcaatattt	gcatgaacct	gctgataagc	catgttgaga	aacaaatata	tctctgacct	240
tctcatcggt	aagcagaggc	tgtagggaac	atggaccata	gcgaanaaaa	aacttagtaa	300
tccaagctgt	tttctacact	gtaaccaggt	ttccaaccaa	ggtggaaatc	tcctataact	360
ggtgcc						366

&lt;210&gt; 216

&lt;211&gt; 260

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

<221> misc\_feature  
 <222> (1)...(260)  
 <223> n = A,T,C or G

```

<400> 216
ctgtataaac agaactccac tgcangaggg agggccgggc caggagaatc tccgcttgtc      60
caagacaggg gcctaaggag ggtctccaca ctgctnntaa gggctnttnc atttttttat      120
taataaaaag tnnaaaaggc ctcttctcaa cttttttccc ttnggctgga aaatttaaaa      180
atcaaaaatt tcctnaagtt ntcaagctat catatatact ntatcctgaa aaagcaacat      240
aattcttctt tccctccttt

```

<210> 217  
 <211> 262  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(262)  
 <223> n = A,T,C or G

```

<400> 217
acctacgtgg gtaagtttan aaatgttata atttcaggaa naggaacgca tataattgta      60
tcttgccat aattttctat ttttaataagg aaatagcaaa ttgggggtggg gggaaatgtag      120
ggcattctac agtttgagca aaatgcaatt aaatgtggaa ggacagcact gaaaaatttt      180
atgaataatc tgtatgatta tatgtctcta gagtagattt ataattagcc acttacccta      240
ataatccttc tgcttgtaaa gt

```

<210> 218  
 <211> 205  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(205)  
 <223> n = A,T,C or G

```

<400> 218
accaagtggt tgcattaccg gaantggatc aangacacca tcgtggccaa cccctgagca      60
cccctatcaa cttcccttttg tagtaaaactt ggaaccttgg aaatgaccag gccaaagactc      120
aggcctcccc agttctactg acctttgtcc ttangtntna ngctccagggt tgcaggaaaa      180
anaaatcagc agacacaggt gtaaa

```

<210> 219  
 <211> 114  
 <212> DNA  
 <213> Homo sapien

```

<400> 219
tactgttttg tctcagtaac aataaataca aaaagactgg ttgtgttccg gccccatcca      60
accacgaagt tgattttctt tgtgtgcaga gtgactgatt ttaaaggaca tgga

```

<210> 220  
 <211> 93

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 220

actagccagc	acaaaaggca	gggtagcctg	aattgctttc	tgctctttac	atttctttta	60
aaataagcat	ttagtgctca	gtccctactg	agt			93

&lt;210&gt; 221

&lt;211&gt; 167

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (167)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 221

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&lt;210&gt; 222

&lt;211&gt; 351

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 222

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taggtgagca	tgattagaga	gcttgtaggt	tgcttttaca	tatatctggc	atatttgagt	300
ctcgatatcaa	aacaatatagat	tggtaaaggt	ggtattattg	tattgataag	t	351

&lt;210&gt; 223

&lt;211&gt; 383

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (383)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 223

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 <212> DNA  
 <213> Homo sapien

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<400> 227

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&lt;210&gt; 228

&lt;211&gt; 744

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 228

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&lt;210&gt; 229

&lt;211&gt; 300

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 229

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cgagtctggg ttttctctat aaagtttgat ccctcctttt ctcatccaaa tcatgtgaac      60
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&lt;210&gt; 230

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 230

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cagcagaaca aatacaataa tgaagagtgc aaagatctca taaaatctat gctgaggaat      60
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&lt;210&gt; 231

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 231

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c						301

&lt;210&gt; 232

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 232

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g						301

&lt;210&gt; 233

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 233

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c						301

&lt;210&gt; 234

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 234

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&lt;213&gt; Homo sapien

&lt;400&gt; 239

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&lt;210&gt; 240

&lt;211&gt; 300

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 240

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&lt;210&gt; 241

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 241

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g						301

&lt;210&gt; 242

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 242

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a						301

&lt;210&gt; 243

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 243

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&lt;210&gt; 244

&lt;211&gt; 300

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 244

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&lt;210&gt; 245

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 245

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&lt;210&gt; 246

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 246

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c						301

&lt;210&gt; 247

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 247

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<400> 250  
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 cttatcttta ttggcttgat aaacataatt atttctaaca ctacgttatt tccagttgcc 120  
 cataagcaca tcagtacttt tctctggctg gaatagtaaa ctaaagtatg gtacatctac 180  
 ctaaaagact actatgtgga ataatacata ctaatgaagt attacatgat ttaaaagacta 240  
 caataaaacc aaacatgctt ataacattaa gaaaaacaat aaagatacat gattgaaacc 300  
 a 301

<210> 251  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 251  
 gccgaggtcc tacattttggc ccagtttccc cctgcacccct ctccagggcc cctgcctcat 60  
 agacaacctc atagagcata ggagaactgg ttgccctggg gccaggggga ctgtctggat 120  
 gccagggggt ctcaaaaatg ccactgtcac tgccaggaaa tgcttctgag cagtacacct 180  
 cattggggtc aatgaaaagc ttcaagaaat ctccaggctc actctcttga aggccccgaa 240  
 cctctggagg ggggcagtggt aatcccagct ccaggacgga tcctgtcgaa aagatatcct 300  
 c 301

<210> 252  
 <211> 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 252

gcaaccaatc actctgtttc acgtgacttt tatcaccata caatttgttg catttcctca	60
ttttctacat tgtagaatca agagtgtaaa taaatgtata tctagtgtct caagaatata	120
tcatttccttt ttcactagga acccattcaa aatataagtc aagaatctta atatacaaa	180
atataatcaag caaactggaa ggcagaataa ctaccataat ttagtataag tacccaaagt	240
tttataaatc aaaagcccta atgataacca tttttagaat tcaatcatca ctgtagaatc	300
a	301

&lt;210&gt; 253

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 253

ttccctaaga agatgttatt ttgttgggtt ttgttccccc tccatctcga ttctcgtacc	60
caactaaaaa aaaaaaataa agaaaaaatg tgctgcgttc tgaaaaataa ctccttagct	120
tggtctgatt gttttcagac cttaaaatat aaacttgttt cacaagcttt aatccatgtg	180
gatttttttt cttagagaac cacaaaacat aaaaggagca agtcggactg aatacctgtt	240
tccatagtgc ccacagggtt ttcctcacat tttctccata ggaaaatgct ttttcccaag	300
g	301

&lt;210&gt; 254

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 254

cgctgcgcct ttcccttggg ggaggggcaa ggccagaggg ggtccaagtg cagcacgagg	60
aacttgacca attcccttga agcgggtggg ttaaaccctg taaatgggaa caaaatcccc	120
ccaaatctct tcactttacc ctggtggact cctgactgta gaattttttg gttgaaacaa	180
gaaaaaaata aagcttttga cttttcaagg ttgcttaaca ggtactgaaa gactggcctc	240
actttaaactg agccaggaaa agctgcagat ttattaatgg gtgtgttagt gtgcagtgcc	300
t	301

&lt;210&gt; 255

&lt;211&gt; 302

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 255

agcttttttt tttttttttt tttttttttt ttcattaaaa aatagtgtct tttattataa	60
attactgaaa tgtttttttt ctgaatataa atataaatat gtgcaaagtt tgacttggat	120
tgggattttt ttgagttctt caagcatctc ctaataacct caagggcctg agtagggggg	180
aggaaaaagg actggagggt gaatctttat aaaaaacaag agtgattgag gcagattgta	240
aacattatta aaaaacaaga aacaacaaaa aaaaatagaga aaaaaaccac cccaacacac	300
aa	302

&lt;210&gt; 256

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 256  
 gttccagaaa acattgaagg tggcttccca aagtctaact agggataccc cctctagcct 60  
 aggaccctcc tccccacacc tcaatccacc aaaccatcca taatgcaccc agataggccc 120  
 acccccaaaa gcctggcacac cttgagcaca cagttatgac caggacagac tcattctcat 180  
 agggaaatag ctgctggcaa actggcatta cctgggtttgt ggggatgggg gggcaagtgt 240  
 gtggcctctc ggcttggtta gcaagaacat tcagggttagg cctaagttaa tcgtgttagt 300  
 t 301

<210> 257  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 257  
 gttgtggagg aactctggct tgctcattaa gtctactga ttttactat cccctgaatt 60  
 tccccactta tttttgtctt tcaatctcgc aggccttaga agaggctcac ctgacctcag 120  
 tcttacctag tccagtctac cccctggagt tagaatggcc atcctgaagt gaaaagtaat 180  
 gtcacattac tcccttcagt gatttcttgt agaagtgcc atccctgaat gccaccaaga 240  
 tccttaattct cacatcttta atcttatctc ttgactcct ctttacaccg gagaaggctc 300  
 c 301

<210> 258  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 258  
 cagcagtagt agatgccgta tgccagcacg cccagcactc ccaggatcag caccagcacc 60  
 agggggcccg ccaccaggcg cagaagcaag ataaacagta ggctcaagac cagagccacc 120  
 cccagggcaa caagaatcca ataccaggac tgggcaaaat cttcaaagat ctttaactgt 180  
 atgtctcggg cattgaggct gtcaataana cgctgatccc ctgctgtatg gtggtgtcat 240  
 tgggtgatccc tgggagcgcc ggtggagtaa cgttgggtcca tggaaagcag cgcccacaac 300  
 t 301

<210> 259  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 259

tcatatatgc	aaacaaatgc	agactangcc	tcaggcagag	actaaaggac	atctcttggg	60
gtgtcctgaa	gtgatttggg	cccctgaggg	cagacaccta	agtaggaatc	ccagtgggaa	120
gcaaagccat	aaggaagccc	aggattcctt	gtgatcagga	agtggggccg	gaaggctctg	180
tccāgctcac	atctcatctg	catgcagcac	ggaccggatg	cgcccactgg	gtcttggctt	240
ccctcccatc	ttctcaagca	gtgtccttgt	tgagccattt	gcctccttgg	ctccagggtg	300
c						301

<210> 260  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 260						
ttttttttct	ccctaaaggaa	aaagaaggaa	caagtctcat	aaaaccaa	aagcaatggt	60
aagggtgtct	aacttgaaaa	agattagggg	tcaactgggtt	acaagttata	attgaatgaa	120
agaactgtaa	cagccacagt	tggccatttc	atgccaatgg	cagcaacaa	caggattaac	180
tagggcaaaa	taaataagtg	tgtggaagcc	ctgataagtg	cttaataaac	agactgatcc	240
actgagacat	cagtaccctg	cggggcgggc	gctcgagccg	aattctgcag	atatccatca	300
c						301

<210> 261  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 261						
aaatattcga	gcaaatcctg	taactaatgt	gtctccataa	aaggctttga	actcagtgaa	60
tctgcttcca	tccacgattc	tagcaatgac	ctctcggaca	tcaaaagctcc	tcttaagggtt	120
agaccaact	attccataca	attcatcagc	aggaaataaa	ggctcttcag	aagggtcaat	180
ggtgacatcc	aattctctct	gataatttag	attcctcaca	accttcctag	ttaagtgaag	240
ggcatgatga	tcattccaaag	cccagtgggc	acttactcca	gacttctgcg	aatgaagatc	300
a						301

<210> 262  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 262						
gaggagagcc	tgttacagca	tttctaagca	cagaatactc	caggagtatt	tgtaattgtc	60
tgtgagcttc	ttgccgcaag	tctctcagaa	atttaaaaag	atgcaaatcc	ctgagtcacc	120
cctagacttc	ctaaaccaga	tcctctgggg	ctggaacctg	gcactctgca	tttghtaatga	180
gggctttctg	gtgcacacct	aattttgtgc	atctttgccc	taaactcctg	attagtgcgc	240
catcattacc	cccacattat	aatgggatag	attcagagca	gatactctcc	agcaagaagt	300
c						301

<210> 263  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 263  
 tttagcttgt ggtaaatgac tcacaaaact gattttaaaa tcaagttaat gtgaattttg 60  
 aaaattacta cttaatccta attcacaata acaatggcat taaggtttga cttgagttgg 120  
 ttcttagtat tatttatggt aaataggctc ttaccacttg caaataactg gccacatcat 180  
 taatgactga cttcccagta aggctctcta aggggtaagt angaggatcc acaggatttg 240  
 agatgctaag gccccagaga tcgtttgac caacctctt attttcagag gggaaaatgg 300  
 g 301

<210> 264  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 264  
 aaagacgtta aaccactcta ctaccacttg tggaactctc aaagggtaaa tgacaaascc 60  
 aatgaatgac tctaaaaaca atatttacct ttaattgggt gtagacaata aaaaaacaag 120  
 gtggatagat ctagaattgt aacattttta gaaaaccata scatttgaca gatgagaaag 180  
 ctcaattata gatgcaaat tataactaaa ctactatagt agtaagaaa tacatttcac 240  
 acccttcata taaattcact atcttggtc gaggcactcc ataaaatgta tcacgtgcac 300  
 a 301

<210> 265  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 265  
 tgcccaagtt atgtgtaagt gtatccgcac ccagaggtaa aactacactg tcatctttgt 60  
 cttcttgta cgcagtattt cttctctggg gagaagccgg gaagtcttct cctggctcta 120  
 catattcttg gaagtctcta atcaactttt gttccatttg ttctatttct tcaggaggga 180  
 ttttcagttt gtcaacatgt tctctaacaa cacttgccca tttctgtaaa gaatccaaag 240  
 cagtcceaagg ctttgacatg tcaacaacca gcataactag agtatccttc agagatacgg 300  
 c 301

<210> 266  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 266  
 taccgtctgc ctttctctcc atccaggcca tctgcgaatc tacatgggtc ctctattctg 60  
 acaccagatc actctttcct ctaccacag gcttgctatg agcaagagac acaacctcct 120  
 ctcttctgtg ttccagcttc ttttctgtt cttcccaccc cttaagtctt attcctgggg 180  
 atagagacac caataccat aacctctctc ctaagcctcc ttataaccga ggggtgcacag 240  
 cacagactcc tgacaactgg taaggccaat gaactgggag ctcacagctg gctgtgcctg 300  
 a 301

<210> 267  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 267  
 aaagagcaca ggccagctca gcctgccctg gccatctaga ctcagcctgg ctccatgggg 60

```

gtttctcagtg ctgagtcctat ccaggaaaaag ctcacctaga ccttctgagg ctgaatcttc      120
atccctcacag gcagcttctg agagcctgat attcctagcc ttgatgggtct ggagtaaagc      180
ctcattctega ttctctctct tcttttcttt caagttggct ttccctcacat cctctctgttc      240
aattcgcttc agcttgctctg ctttagccct catttccaga agcttcttct ctttggcatc      300
t                                                                                   301

```

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<210> 268
<211> 301
<212> DNA
<213> Homo sapien

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```

<400> 268
aatgtctcac tcaactactt cccagcctac cgtggcctaa ttctgggagt tttcttctta      60
gatcttggga gagctgggtc ttctaaggag aaggagggaag gacagatgta accttggatc      120
tcgaagagga agtctaattg aagtaattag tcaacgggtcc ttgtttagac ccttgggaata      180
tgctgggtgg ctccagtggc ccttttggag aaagcaagta ttattcttaa ggagtaacca      240
cttcccatgg ttctactttc taccatcatc aattgtatat tatgtattct ttggagaact      300
a                                                                                   301

```

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<210> 269
<211> 301
<212> DNA
<213> Homo sapien

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```

<400> 269
taacaatata cactagctat ctttttaact gtccatcatt agcaccaatg aagattcaat      60
aaaattacct ttattcacac atctcaaaac aattctgcaa attcttagtg aagtttaact      120
atagtcacag accttaaaata ttccattgtt ttcttatgtc tactgaaaat aagttcacta      180
cttttctgga tattctttac aaaatcttat taaaattcct ggtattatca cccccaatta      240
tacagtagca caaccacctt atgtagtttt tacatgatag ctctgtagaa gtttcacatc      300
t                                                                                   301

```

```

<210> 270
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 270
cattgaagag cttttgcgaa acatcagaac acaagtgcct ataaaattaa ttaagcctta      60
cacaagaata catattcctt ttatttctaa ggagttaaac atagatgtag ctgatgtgga      120
gagcttgctg gtgcagtgca tattggataa cactattcat ggccgaattg atcaagtcac      180
ccaactcctt gaactggatc atcagaagaa ggggtgggtgca cgatatactg cactagataa      240
tggaccaacc aactaaattc tctcaccagg ctgtatcagt aaactggcct aacagaaaac      300
a                                                                                   301

```

```

<210> 271
<211> 301
<212> DNA
<213> Homo sapien

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```

<220>
<221> misc_feature
<222> (1)... (301)
<223> n = A,T,C or G

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<400> 271  
 aaaaggttct cataagatta acaattttaa taaatatttg atagaacatt ctttctcatt 60  
 ttatatgctc atcttttaggg ttgatattca gttcatgctt cccttgctgt tcttgatcca 120  
 gaattgcaat cacttcatca gccgttatc gctccaattc tctataaagt ggggtccaagg 180  
 tgaaccacag agccacagca cactcttttc ccttggtgac tgccttcacc ccatganggt 240  
 tctctctcc agatganaac tgatcatgcg cccacatttt gggttttata gaagcagtca 300  
 c 301

<210> 272  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 272  
 taaattgcta agccacagat aacaccaatc aaatggaaca aatcactgtc ttcaaagtgc 60  
 ttatcagaaa accaaatgag cctggaatct tcataatacc taaacatgcc gtatttagga 120  
 tccaataaatt ccctcatgat gagcaagaaa aattctttgc gcacccctcc tgcattccaca 180  
 gcatcttttc caacaaatat aaccttgagt ggctcttctg aatctatggt ctttgttttc 240  
 ctaaggactt ccattgcac tctacaata tttctctac gcaccactag aattaagcag 300  
 g 301

<210> 273  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (301)  
 <223> n = A,T,C or G

<400> 273  
 acatgtgtgt atgtgtatct ttgggaaaaa aanaagacat cttgtttayt attttttttg 60  
 agagangctg ggacatggat aatcacwtaa tttgctayta tyactttaat ctgactygaa 120  
 gaaccgtcta aaaataaaat ttaccatgct dtatattcct tatagtatgc ttatttcacc 180  
 ttttttctgt ccagagagag tatcagtgac ananatttma ggggtgaamac atgmattggg 240  
 gggacttnty ttacngagm accctgcccg sgcgccctcg makcngantt ccgcsananc 300  
 t 301

<210> 274  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (301)  
 <223> n = A,T,C or G

<400> 274  
 cttatatact ctttctcaga ggcaaaagag gagatgggta atgtagacaa ttctttgagg 60  
 aacagtaaat gattattaga gagaangaat ggaccaagga gacagaaatt aacttgtaaa 120  
 tgattctctt tggaatctga atgagatcaa gagggcagct ttagcttggtg gaaaagtcca 180  
 tctaggtatg gttgcattct cgtcttcttt tctgcagtag ataatgaggt aaccgaaggc 240  
 aattgtgctt ctttgcataa gaagctttct tggtcataac aggaatttcc aganaaagtc 300



c

301

<210> 275  
<211> 301  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(301)  
<223> n = A,T,C or G

&lt;400&gt; 275

tcggtgtcag cagcacgtgg cattgaacat tgcaatgtgg agcccaaacc acagaaaatg	60
gggtgaaatt ggccaacttt ctattaactt atgttggcaa ttttgccacc aacagtaagc	120
tggcccttct aataaaagaa aattgaaagg tttctcacta aacggaatta agtagtggag	180
tcaagagact ccagagcctc agcgtacctg cccgggcggc cgctcgaagc cgaattctgc	240
agatatccat cacactggcg gncgctcgan catgcatcta gaaggnccaa ttcgccctat	300
a	301

<210> 276  
<211> 301  
<212> DNA  
<213> Homo sapien

&lt;400&gt; 276

tgtacacata ctcaataaat aaatgactgc attgtggtat tattactata ctgattatat	60
ttatcatgtg acttctaatt agaaaatgta tccaaaagca aaacagcaga tatacaaaat	120
taaagagaca gaagatagac attaacagat aaggcaactt atacattgag aatccaaatc	180
caatacatct aaacatttgg gaaatgaggg ggacaaatgg aagccagatc aaatttgtgt	240
aaaactattc agtatgtttc ccttgcttca tgtctgagaa ggctctcctt caatggggat	300
g	301

<210> 277  
<211> 301  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(301)  
<223> n = A,T,C or G

&lt;400&gt; 277

tttgttgatg tcagtatttt attacttgcg ttatgagtgc tcacctggga aattctaaag	60
atacagagga cttggaggaa gcagagcaac tgaattttaat ttaaaagaag gaaaacattg	120
gaatcatggc actcctgata ctttcccaaa tcaacactct caatgcccca ccctcgtcct	180
caccatagtg gggagactaa agtggccacg gatttgcctt angtggtcag tgcgttctga	240
gttcnctgtc gattacatct gaccagtctc ctttttccga agtcnctccg ttcaattcttg	300
c	301

<210> 278  
<211> 301  
<212> DNA  
<213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 278  
 taccactaca ctccagcctg ggcaacagag caagacctgt ctcaaagcat aaaatggaat 60  
 aacatatcaa atgaaacagg gaaaatgaag ctgacaattt atggaagcca gggcttgtca 120  
 cagtctctac tgttattatg cattacctgg gaatttatat aagcccttaa taataatgcc 180  
 aatgaacatc tcatgtgtgc tcacaatggt ctggcactat tataagtgtc tcacagggtt 240  
 tatgtgttct tcgtaacttt atggantagg tactcggccg cgaacacgct aagccgaatt 300  
 c 301

<210> 279  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 279  
 aaagcaggaa tgacaaagct tgcttttctg gtatgttcta ggtgtattgt gacttttact 60  
 gttatattaa ttgccaatat aagtaaatat agattatata tgtatagtgt ttcacaaagc 120  
 ttagaccttt accttccagc caccaccacag tgcttgatat ttcagagtca gtcattgggt 180  
 atacatgtgt agttccaaag cacataagct agaanaanaa atatttctag ggagcactac 240  
 catctgtttt cacatgaaat gccacacaca tagaactcca acatcaattt cattgcacag 300  
 a 301

<210> 280  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 280  
 ggtactggag ttctcctccc ctgtgaaaac gtaactactg ttgggagtga attgaggatg 60  
 tagaagagtg gtggaaccaa atttgtgtca atggaaatag gagaatatgg ttctcactct 120  
 tgagaaaaaa acctaaagatt agcccaggta gttgcctgta acttcagttt ttctgcctgg 180  
 gtttgatata gtttaggggt ggggttagat taagatctaa attacatcag gacaaagaga 240  
 cagactatta actccacagt taattaagga ggtatgttcc atgtttattt gttaaagcag 300  
 t 301

<210> 281  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 281  
 aggtacaaga aggggaatgg gaaagagctg ctgctgtggc attgttcaac ttgatatttc 60  
 gccgagcaat ccaaatcctg aatgaagggg catcttctga aaaaggagat ctgaatctca 120  
 atgtggttagc aatgggttata tcgggttata cggatgagaa gaactccctt tggagagaaa 180  
 tgtgttagcac actgcgatta cagctaaata acccgatttt gtgtgtcatg tttgcatttc 240

tgacaagtga aacaggatct tacgatggag ttttgtatga aaacaaagt gcagtacctc 300  
g 301

<210> 282  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 282  
cagggtactac agaattaaaa tactgacaag caagtagttt ctggcgctgc acgaattgca 60  
tccagaaccc aaaaattaag aatccaata agacattttg tgggcacctg ctgacacaga 120  
agcgacagaag caaagccagc gcagaacat gtaacctta cagctcagcc tgcacagaag 180  
cgcagaagca aagcccgagc agaaccatgc taaccttaca gctcagcctg cacagaagcg 240  
cagaagcaaa gcccgagcag aacatgctaa ccttacagct cagcctgcac agaagcacag 300  
a 301

<210> 283  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 283  
atctgtatac ggcagacaaa ctttatarag tgtagagagg tgagcgaaag gatgcaaaag 60  
cactttgagg gctttataat aatatgctgc ttgaaaaaaa aaatgtgtag ttgatactca 120  
gtgcatctcc agacatagta aggggttgct ctgaccaatc aggtgatcat tttttctatc 180  
acttcccagg ttttatgcaa aaattttggt aaattctata atggtgatat gcattcttta 240  
ggaaacatat acatttttaa aaattctatt tatgtaagaa ctgacagacg aatttgcctt 300  
g 301

<210> 284  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 284  
cagggtacaaa acgctattaa gtggcttaga atttgaacat ttgtggtctt tatttacttt 60  
gcttcgtgtg tgggcaaaagc aacatcttcc cttaaataat attaccaaga aaagcaagaa 120  
gcagattagg tttttgacaa aacaacacag ccaaaagggg gctgacctgg agcagagcat 180  
ggtgagaggc aaggcatgag agggcaagtt tgttgtggac agatctgtgc ctactttatt 240  
actggagtaa aagaaaaaaa agttcattga tgtcgaagga tatatacagt gttagaatt 300  
a 301

<210> 285  
<211> 301  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)... (301)  
<223> n = A,T,C or G

<400> 285  
acatcaccat gatcggatcc cccaccatt atacgttgta tgtttacata aatactcttc 60  
aatgatcatt agtggtttta aaaaaatact gaaaaactct tctgcacccc aatctctaac 120

```

caggaaagca aatgctatct acagacctgc aagccctccc tcaaacnaaa ctatttctgg 180
attaaaatag tctgacttct tttagaggtca cagactagg caaatgctat ttacgatctg 240
caaaagctgt ttgaagagtc aaagcccca tgtgaacacg atttctggac cctgtaacag 300
t                                                    301

```

```

<210> 286
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 286
taccactgca ttccagcctg ggtgacagag tgagactccg tctccaaaaa aaactttgct 60
tgtatattat ttttgcctta cagtggatca ttctagtagg aaaggacagt aagatttttt 120
atcaaaatgt gtcattgccag taagagatgt tatattcttt tctcatttct tccccaccca 180
aaaataagct accatatagc ttataagctc caaatttttg ccttttacta aaatgtgatt 240
gtttctgttc attgtgtatg cttcatcacc tatattaggc aaattccatt ttttcccttg 300
t                                                    301

```

```

<210> 287
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 287
tacagatctg ggaactaaat attaaaaatg agtgtggctg gatatatgga gaatgttggg 60
cccagaagga acgtagagat cagatattac aacagctttg ttttgagggt tagaaaatag 120
aaatgatttg gttatgaacg cacagtttag gcagcagggc cagaatcctg accctctgcc 180
ccgtgggtat ctccctcccc gcttggctgc ctcattgtat cacagtattc cattttgttt 240
gttgcatgtc ttgtgaagcc atcaagattt tctcgtctgt tttcctctca ttggaatgc 300
t                                                    301

```

```

<210> 288
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 288
gtacacctaa ctgcaaggac agctgaggaa tgtaatgggc agccgctttt aaagaagtag 60
agtcaatagg aagacaaaat ccagttccag ctcagtctgg gtatctgcaa agctgcaaaa 120
gatctttaa gacaatttca agagaatatt tccttaaagt tggcaatttg gagatcatc 180
aaaagcatct gcttttgtga tttaatttag ctcattctgc cactggaaga atccaaacag 240
tctgccttaa ttttgatga atgcatgatg gaaattcaat aatttagaaa gttaaaaaaa 300
a                                                    301

```

```

<210> 289
<211> 301
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

```

```

<400> 289

```

ggtagactgt	tttcaatgta	tgtttctaca	cattgctacc	tcagtgctcc	tggaaactta	60
gcttttgatg	tttccaagct	gtgccacctc	atttaacttc	tgaaaactgt	atcacctttg	120
ccaagtaaga	gtgggtgcct	atttcagctg	cttgcagaaa	atgactggct	cctgacttaa	180
cgttctataa	atgaatgtgc	tgaagcaaag	tgcccatggg	ggcggcgaan	aagagaaaga	240
tgtgttttgt	tttggaactc	ctgtgggtcc	ttccaatgct	gtgggtttcc	aaccagnnga	300
a						301

<210> 290

<211> 301

<212> DNA

<213> Homo sapien

**<220>**

&lt;221&gt; misc feature

 $\langle 222 \rangle \quad (1) \dots (301)$ 

<223> n = A, T, C or G

<400> 290

acactgagct	cttcttgata	aatatacaga	atgcttgcca	tatacaagat	tctatactac	60
tgactgaatc	gttctattct	ctcacagctc	ttacccccc	aagcttttcc	accctaaagt	120
ttctgacctc	tttctttaat	cacagtaggg	atagaggcag	ancacctac	aatgaacatg	180
gagttctatc	aagaggcaga	aacagcacag	aatcccagtt	ttaccattcg	ctagcagtcg	240
tgccctgaac	aaaaacattt	ctccatgtct	cattttcttc	atgcctcaag	taacagtgag	300
a						301

<210> 291

<211> 301

## <212> DNA

<213> Homo sapien

&lt;400&gt; 291

caggtagccaa	tttcttctat	cctagaagaaca	tttcatttta	tgtgtgttgaa	acataacaac	60
tatatcagct	agattttttt	ttctatgcttt	aactgcgtat	gaaattttga	cacattctgc	120
tttaaccttt	tgtttatag	tgaatcacaa	aatgtatttt	tatgtattct	gtagtctaat	180
agccatggct	gtttacttca	tttaatttat	ttagcataaa	gacattatga	aaaggcctaa	240
acatgagctt	cacttcccca	ctaactaatt	agcatctgtt	attttttaac	cgtaatgcct	300
a						301

<210> 292

<211> 301

<212> DNA

<213> Homo sapien

**<220>**

<221> misc feature

 $\langle 222 \rangle \quad (1) \dots (301)$ 

<223> n = A, T, C or G

<400> 292

accttttagt	agtaaatgtct	aataataaat	aagaaatcaa	ttttataagg	tccatatagc	60
tgtattcaat	aatttttcaa	tttcaaaagt	aaatatccat	catttttaaa	gttgggattc	120
aataacaaag	natataaccg	aaggaaaaaa	cagatgagac	ataaaaatga	tgcngnagatg	180
ggaatatatg	tasttyatga	atgttntatta	aattccagtt	ataatagtgg	ctacacactg	240
tctactacaa	cacagagccc	acagtcctat	atgccacaaa	cacatttcca	taacttgaaa	300
a						301

<210> 293  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 293  
 ggtaccaagt gctgggtgcc gccctgttacc tgtttctcact gaaaagtctg gctaagtctc 60  
 ttgtgtagtc actttctgatt ctgacaatca atcaatcaat ggccctagagc actgactgtt 120  
 aacacaaacg tcactagcaa agtagcaaca gctttaagtc taaatacaaa gctgttctgt 180  
 gtgagaattt tttaaaaggc tacttgtata ataacccttg tcatttttaa tgtacctcgg 240  
 ccgcgaccac gctaagccga attctgcaga tatccatcac actggcggcc gctcgagcat 300  
 g 301

<210> 294  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 294  
 tgacccataa caatatacac tagctatctt tttaactgtc catcattagc accaatgaag 60  
 attcaataaa attaccttta ttcacacatc tcaaaaacaat tctgcaaatt cttagtgaag 120  
 tttaactata gtcacaganc ttaaatattc acattgtttt ctatgtctac tgaaaataag 180  
 ttcactactt ttctgggata ttctttacaa aatcttatta aaattcctgg tattatcacc 240  
 cccaattata cagtagcaca accaccttat gtagttttta catgatagct ctgtagaggt 300  
 t 301

<210> 295  
 <211> 305  
 <212> DNA  
 <213> Homo sapien

<400> 295  
 gtactctttc tctccctccc tctgaattta attctttcaa cttgcaattt gcaaggatta 60  
 cacatttcac tgtgatgtat attgtgttgc aaaaaaaaaa gtgtctttgt ttaaaattac 120  
 ttggttttgt aatccattct gctttttccc cattggaact agtcattaac ccattctctga 180  
 actggttagaa aaacrtctga agagctagtc tatcagatc tgacagggtga attggatggg 240  
 tctcagaacc atttcaccca gacagcctgt tttctatcctg ttttaataaat tagtttgggt 300  
 tctct 305

<210> 296  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 296  
 aggtactatg ggaagctgct aaaataatat ttgatagtaa aagtatgtaa tgtgctatct 60  
 cacctagtag taaactaaaa ataaactgaa actttatgga atctgaagtt attttccttg 120  
 attaaataga attaataaac caatatgagg aaacatgaaa ccattgcaatc tactatcaac 180  
 tttgaaaaag tgattgaacg aaccacttag ctttcagatg atgaacactg ataagtcatt 240

tgctattact ataaatttta aaatctgtta ataagatggc ctataggag gaaaaagggg 300  
c 301

<210> 297

<211> 300

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (300)

<223> n = A,T,C or G

<400> 297

actgagtttt aactggagcg caagcaggca aggctggaag gttttgctct ctttggtgcta 60  
aagggttttga aaaccttgaa ggagaatcat ttgacaaga agtacttaag agtctagaga 120  
acaaagangt gaaccagctg aaagctctcg ggggaanctt acatgtgttg ttaggcctgt 180  
tccatcattg ggagtgacct ggccatccct caaaatttgt ctgggctggc ctgagtggc 240  
accgcacctc ggccgcgacc acgctaagcc gaattctgca gatatccatc aactggcg 300

<210> 298

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (301)

<223> n = A,T,C or G

<400> 298

tatggggttt gtcacccaaa agctgatgct gagaaaggcc tccctggggc ccctcccgcg 60  
ggcatctgag agacctggcg ttccagtgtt tctggaaatg ggtcccagtg ccgcccgtg 120  
tgaagctctc agatcaatca cgggaaggcg ctggcggtgg tggccacctg gaaccaccct 180  
gtcctgtctg ttacatttc actaycagggt tttctctggg cattacnatt tgttccceta 240  
caacagtgc ctgtgcattc tgctgtggcc tgctgtgtct gcagggtggc ctcagcgagg 300  
t 301

<210> 299

<211> 301

<212> DNA

<213> Homo sapien

<400> 299

gttttgagac ggagtttcac tcttgttgcc cagactggac tgcaatggca gggtctctgc 60  
tcactgcacc ctctgcctcc caggttcgag caattctcct gcctcagcct cccaggtagc 120  
tgggattgca ggctcacgcc accataccca gctaattttt ttgtattttt agtagagacg 180  
gagtttcgcc atgttggcca gctggtctca aactcctgac ctcaagcgac ctgcctgcct 240  
cggcctccca aagtgtgga attataggca tgagtcaaca cgcccagcct aaagatatct 300  
t 301

<210> 300

<211> 301

<212> DNA

<213> Homo sapien

<400> 300  
 attcagtttt atttgctgcc ccagtatctg taaccaggag tggcacaata tcttgccaga 60  
 tatgtcccac acccactggg aaaggctccc acctggctac ttcctctatc agctgggtca 120  
 gctgcattcc acaagggtct cagcctaatt agtttcaacta cctggcagtc tcaaaactta 180  
 gtaaagcaag accatgacat tccccacgg aaatcagagt ttgccccacc gtcttgttac 240  
 tataaagcct gcctctaaca gtcttgcctt cttcacacca atcccagagc catcccccat 300  
 g 301

<210> 301  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 301  
 ttaaatTTTT gagaggataa aaaggacaaa taatctagaa atgtgtcttc ttcagtctgc 60  
 agaggacccc aggtctccaa gcaaccacat ggtcaagggc atgaataatt aaaagttggg 120  
 gggaaactcac aaagaccctc agagctgaga caccacaac agtgggagct cacaagagacc 180  
 ctcaagctg agacaccac aacagtggga gtcacaaaag accctcagag ctgagacacc 240  
 cacaacagca cctcgttcag ctgccacatg tgtgaataag gatgcaatgt ccagaagtgt 300  
 t 301

<210> 302  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 302  
 aggtacacat ttagcttctg gtaaatgact cacaaaaactg attttaaaat caagttaatg 60  
 tgaatttga aaattactac ttaattctaa ttcacaataa caatggcatt aagggttgac 120  
 ttgagttggg tcttagtatt atttatggta aataggctct taccacttgc aaataactgg 180  
 ccacatcatt aatgactgac ttcccagtaa ggctctctaa ggggtaagta ggaggatcca 240  
 caggatttga gatgctaagg ccccagagat cgtttgatcc aaccctctta ttttcagagg 300  
 g 301

<210> 303  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 303  
 aggtaccaac tgtggaaata ggtagaggat cattttttct ttccatatca actaagttgt 60  
 atattgtttt ttgacagttt aacacatctt cttctgtcag agattctttc acaatagcac 120  
 tggctaattg aactaccgct tgcattgtaa aaatgggtgt ttgtgaaatg atcataggcc 180  
 agtaacgggt atgtttttct aactgatctt ttgtctgttc caaagggacc tcaagacttc 240  
 catcgatttt atatctgggg tctagaaaag gagttaatct gttttccctc ataaattcac 300  
 c 301

<210> 304  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 304  
 acatggatgt tatTTTgcag actgtcaacc tgaatttga tttgcttgac attgcctaatt 60



tattagtttc agtttcagct taccactttt ttgtctgcaa catgcaraas agacagtgcc	120
cttttttagtg tatcatatca ggaatcatct cacattggtt tgtgccatta ctggtgcagt	180
gactttcagc cacttgggta aggtggagtt ggccatatgt ctccactgca aaattactga	240
ttttcctttt gtaattaata agtgtgtgtg tgaagattct ttgagatgag gtatatatct	300
c	301

<210> 305  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 305	
gangtacagc gtggtcaagg taacaagaag aaaaaaatgt gagtggcatc ctgggatgag	60
cagggggaca gacctggaca gacacgttgt catttgctgc tgtgggtagg aaaatgggag	120
taaaggagga gaaacagata caaatctccc aactcagtat taagggtattc tcatgcctag	180
aatattggta gaaacaagaa tacattcata tggcaataaa ctaaccatgg tggacaacaaa	240
ttctgggatt taagttggat accaangaaa ttgtattaaa agagctgttc atggaataag	300
a	301

<210> 306  
 <211> 8  
 <212> PRT  
 <213> Homo sapien

<400> 306  
 Val Leu Gly Trp Val Ala Glu Leu  
 1 5

<210> 307  
 <211> 637  
 <212> DNA  
 <213> Homo sapien

<400> 307	
acaggggatg aagggaagg gagaggatga ggaagccccc ctggggattt gggttggctcc	60
ttgtgatcag gtggtctatg gggcttatcc ctacaaagaa gaatccagaa ataggggcac	120
attgaggaat gatacttgag cccaaagagc attcaatcat tgttttattt gccttmtttt	180
cacaccattg gtgagggagg gattaccacc ctgggggttat gaagatgggt gaacacccca	240
cacatagcac cggagatatg agatcaacag ttctcttagcc atagagattc acagcccaga	300
gcaggaggac gcttgccacac catgcaggat gacatggggg atgcgctcgg gattggtgtg	360
aagaagcaag gactgttaga ggcaggcttt atagtacaa gacggtgggg caaactctga	420
tttccgtggg ggaatgtcat ggtcttgcct tactaagttt tgagactggc aggtagtga	480
actcattagg ctgagaacct tgtggaatgc acttgaccca sctgatagag gaagtagcca	540
ggtgggagcc ttcccagtg ggtgtgggac atatctggca agattttgtg gcactcctgg	600
ttacagatag tggggcagca aataaaactg aatcttg	637

<210> 308  
 <211> 647  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(647)  
 <223> n = A,T,C or G

<400> 308  
 acgattttca ttatcatgta aatcgggtca ctcaaggggc caaccacagc tgggagccac 60  
 tgctcagggg aaggttcata tgggactttc tactgcccaa ggttctatac aggatataaa 120  
 ggngcctcac agtatagatc tggtagcaaa gaagaagaaa caaacactga tctctttctg 180  
 ccacccctct gaccctttgg aactcctctg accctttaga acaagcctac ctaatatctg 240  
 ctagagaaaa gaccaacaac ggctcaaa gatctcttac catgaagggtc tcagctaatt 300  
 cttggctaag atgtgggttc cacattaggt tctgaatatg gggggaagggt tcaatttgct 360  
 cattttgtgt gtggataaag tcaggatgcc caggggccag agcagggggc tgcttgcttt 420  
 gggaaacaatg gctgagcata taaccatagg ttatggggaa caaaacaaca tcaagtcac 480  
 tgtatcaatt gccatgaaga ctgaggggac ctgaatctac cgattcatct taaggcagca 540  
 ggaccagttt gagtggcaac aatgcagcag cagaatcaat ggaaacaaca gaatgattgc 600  
 aatgtcctct ttttctcct gcttctgact tgataaaagg ggaccgt 647

<210> 309  
 <211> 460  
 <212> DNA  
 <213> Homo sapien

<400> 309  
 accttatagt ttaggctgga cattggaaaa aaaaaaagc cagaacaaca tgtgatagat 60  
 aatatgattg gctgcacact tccagactga tgaatgatga acgtgatgga ctattgtatg 120  
 gagcacatct tcagcaagag ggggaaatac tcatcatttt tggccagcag ttgtttgatc 180  
 accaaacatc atgccagaat actcagcaaa ccttcttagc tcttgagaag tcaaatgccg 240  
 ggggaattta ttccctggcaa ttttaattgg actccttatg tgagagcagc ggctaccccg 300  
 ctggggtcgtt ggagcgaaac cgtcactagt ggacatgcag tggcagagct cctggtaacc 360  
 acctagagga atacacaggg acatgtgtga tgccaagcgt gacacctgta gactcaaat 420  
 ttgtcttgtt tttgtcttcc ggtgtgtaag attcttaagt 460

<210> 310  
 <211> 539  
 <212> DNA  
 <213> Homo sapien

<400> 310  
 acgggactta tcaaataaag ataggaaaa aagaaaactc aaatattata ggcagaaatg 60  
 ctaagggttt taaaatatgt caggattgga agaaggcatg gataaagaac aaagttcagt 120  
 taggaaagag aaacacagaa ggaagagaca caataaaagt cattatgtat tctgtgagaa 180  
 gtcagacagt aagattttgt ggaaatgggt tggtttgttg tatgggtatgt attttagcaa 240  
 taatctttat ggcagagaaa gctaaaatcc tttagcttgc gtgaatgatc acctgctgaa 300  
 ttctcaagg taggcagatg gaaggagggt ttagaggaga cacagacaca atgaactgac 360  
 ctagatagaa agccttagta tactcagcta ggaatagtga ttctgagggc acactgtgac 420  
 atgattatgt cattacatgt atggtagtga tggggatgat aggaagggaag aacttatggc 480  
 atattttcac ccccaaaaa gtcagttaaa tattgggaca ctaaccatcc aggtcaaga 539

<210> 311  
 <211> 526  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(526)  
 <223> n = A,T,C or G

<400> 311  
 caaatttgag ccaatgacat agaattttac aaatcaagaa gcttattctg gggccatttc 60  
 ttttgacgtt ttctctaaac tactaaagag gcattaatga tccataaatt atattatcta 120  
 cattaccagc atttaaaatg tgttcagcat gaaatattag ctacagggga agctaaaataa 180  
 attaaacatg gaataaagat ttgtccttaa atataatcta caagaagact ttgatatttg 240  
 tttttcacaa gtgaagcatt cttataaagt gtcataacct ttttggggaa actatgggaa 300  
 aaaaatgggga aactctgaag ggttttaagt atcttacctg aagctacaga ctccataacc 360  
 tctctttaca gggagctcct gcagccccta cagaaatgag tggctgagat tcttgattgc 420  
 acagcaagag cttctcatct aaacccttcc cctttttagt atctgtgtat caagtataaa 480  
 agttctataa actgtagtnt acttatttta atcccaaaag cacagt 526

<210> 312  
 <211> 500  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(500)  
 <223> n = A,T,C or G

<400> 312  
 cctctctctc cccaccccc gactctagag aactgggttt tctccagta ctccagcaat 60  
 tcattttctga aagcagttga gccactttat tccaaagtac actgcagatg ttcaaaactct 120  
 ccattttctct ttcccttcca cctgccagtt ttgctgactc tcaacttgtc atgagtgtaa 180  
 gcattaaagga cattatgctt cttcgattct gaagacaggc cctgctcatg gatgactctg 240  
 gcttcttagg aaaatatattt tcttccaaaa tcagtaggaa atctaaactt atccccctctt 300  
 tgcagatgtc tagcagcttc agacatttgg ttaagaacct atgggaaaaa aaaaaatcct 360  
 tgctaattgt gtttctcttg taaaccanga ttcttatttg nctggtatag aatatcagct 420  
 ctgaacgtgt ggtaaaagatt tttgtgttg aatataggag aaatcagttt gctgaaaaatg 480  
 tagtcttaat tatctatttg 500

<210> 313  
 <211> 718  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(718)  
 <223> n = A,T,C or G

<400> 313  
 ggagatttgt gtggtttgca gccgagggag accaggaaga tctgcatggt ggaagaggac 60  
 tgatgataca gaggtgagaa ataagaaagg ctgctgactt taccatctga ggccacacat 120  
 ctgctgaaat ggagataatt aacatcacta gaaacagcaa gatgacaata taatgtctaa 180  
 gtagtacat gtttttgac atttccagcc cttttaaata tccacacaca cagggaagcac 240  
 aaaaggaagc acagagatcc ctgggagaaa tgcccggccg ccactcttgg tcatcgatga 300  
 gcctcgccct gtgcctgntc ccgcttgta ggaagggaca ttagaaaaatg aattgatgtg 360  
 ttccttaaag gatggcagga aaacagatcc tgttctggat atttatttga acgggattac 420

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agatttgaaa tgaagtcaca aagtgagcat taccaatgag aggaaaacag acgagaaaat 480
cttgatggtt cacaagacat gcaacaaaca aaatggaata ctgtgatgac acgagcagcc 540
aactggggag gagataccac ggggcagagg tcaggattct ggccctgctg cctaactgtg 600
cgttatacca atcattttcta tttctaccct caaacaagct gtngaataac tgacttacgg 660
ttctnttggc ccacattttc atnatccacc cntcntttt aannttantc caaantgt 718

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&lt;210&gt; 314

&lt;211&gt; 358

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 314

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cataatcaaa tatagctgta gtacatgttt tcattggtgt agattaccac aaatgcaagg 120
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&lt;210&gt; 315

&lt;211&gt; 341

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 315

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&lt;210&gt; 316

&lt;211&gt; 151

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 316

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agactgggca agactcttac gccccacact gcaatttggt ctgtgtgccc tatccattta 60
tgtgggcctt tctcgagttt ctgattataa acaccactgg agcgatgtgt tgactggact 120
cattcaggga gctctggttg caatattagt t 151

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&lt;210&gt; 317

&lt;211&gt; 151

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 317

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agaactagtg gatcctaatt aaatacctga aacatatatt ggcatttata aatggctcaa 60
atcttcattt atctctggcc ttaaccttgg ctccctgaggc tgcggccagc agatcccagg 120
ccagggtctt gttcttgcca cacctgcttg a 151

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&lt;210&gt; 318

&lt;211&gt; 151

&lt;212&gt; DNA

<213> Homo sapien

<400> 318

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<210> 319

<211> 151

<212> DNA

<213> Homo sapien

<400> 319

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taagattggg tttatgtgat tttagtgggt a	151

<210> 320

<211> 150

<212> DNA

<213> Homo sapien

<400> 320

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<210> 321

<211> 151

<212> DNA

<213> Homo sapien

<400> 321

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<210> 322

<211> 151

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(151)

<223> n = A,T,C or G

<400> 322

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<210> 323

<211> 151

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(151)

<223> n = A,T,C or G

<400> 323

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gttcaatyaa aaagacactt ancccatgtg g	151

<210> 324

<211> 461

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(461)

<223> n = A,T,C or G

<400> 324

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<210> 325

<211> 400

<212> DNA

<213> Homo sapien

<400> 325

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<210> 326

<211> 1215

<212> DNA

<213> Homo sapien

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&lt;210&gt; 327

&lt;211&gt; 220

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 327

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1      5      10      15
Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp Val
20     25     30
Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly
35     40     45
Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu
50     55     60
Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu Ala
65     70     75     80
Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser Asp
85     90     95
Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly Asn
100    105    110
Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met Pro
115    120    125
Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu Val Cys
130    135    140
Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala Gly
145    150    155    160
Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly Pro
165    170    175
Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys Ala
180    185    190
Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu Cys Lys
195    200    205
Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
210    215    220

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&lt;210&gt; 328

<211> 234  
 <212> DNA  
 <213> Homo sapien

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 atccgcagtg ggtgctgtca gccacacact gttccagaa ctcctacacc atcgggctgg 180  
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<210> 329  
 <211> 77  
 <212> PRT  
 <213> Homo sapien

<400> 329  
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 Phe Cys Ser Gly Val Leu Val His Pro Gln Trp Val Leu Ser Ala Thr  
 35 40 45  
 His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly Leu His Ser Leu  
 50 55 60  
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<210> 330  
 <211> 70  
 <212> DNA  
 <213> Homo sapien

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<210> 331  
 <211> 22  
 <212> PRT  
 <213> Homo sapien

<400> 331  
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 Val Ser Gly Ser Cys Ser  
 20

<210> 332  
 <211> 2507  
 <212> DNA  
 <213> Homo sapien

<400> 332  
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&lt;210&gt; 333

&lt;211&gt; 3030

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 333

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<210> 334  
 <211> 2417  
 <212> DNA  
 <213> Homo sapien

<400> 334						
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&lt;210&gt; 335

&lt;211&gt; 2984

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 335

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&lt;210&gt; 336

&lt;211&gt; 147

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 336

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20          25          30
Pro Lys Gln Pro Gln Lys Arg Ser Arg Ala Ala Phe Ser His Thr Gln
35          40          45
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Pro Glu Arg Ala His Leu Ala Lys Asn Leu Lys Leu Thr Glu Thr Gln
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 Gly Ala Arg Val Tyr Leu Ala Cys Arg Asp Val Glu Lys Gly Glu Leu  
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 Val Ala Lys Glu Ile Gln Thr Thr Thr Gly Asn Gln Gln Val Leu Val  
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                     100                    105                    110  
 Gly Phe Leu Ala Glu Glu Lys His Leu His Val Leu Ile Asn Asn Ala  
                     115                    120                    125  
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 His Ile Gly Val Asn His Leu Gly His Phe Leu Leu Thr His Leu Leu



&lt;400&gt; 342

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&lt;210&gt; 343

&lt;211&gt; 382

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 343

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&lt;210&gt; 344

&lt;211&gt; 536

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 344

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&lt;210&gt; 345

&lt;211&gt; 251

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 345

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 <223> n = A,T,C or G

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251

&lt;210&gt; 350

&lt;211&gt; 908

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 350

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&lt;211&gt; 472

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 351

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&lt;210&gt; 352

&lt;211&gt; 251

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 352

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&lt;210&gt; 353

&lt;211&gt; 436

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 353

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&lt;210&gt; 354

&lt;211&gt; 854

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 354

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acacgggatg	tcag					854

&lt;210&gt; 355

&lt;211&gt; 676

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 355

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&lt;210&gt; 356

&lt;211&gt; 574

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 356

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&lt;210&gt; 357

&lt;211&gt; 393

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 357

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taatatggkg	kcttggtcac	tatacttaaa	aatgcaccac	tcataaatat	ttaatccagc	120
aagccacac	caaracttga	ttttatcaac	aaaaaccct	aaatataaac	ggsaaaaaag	180
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gcataatctg	tacaaaatta	aactgtcctt	tttggcattt	taacaaattt	gcaacgktct	360
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&lt;210&gt; 358

&lt;211&gt; 630

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 358

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caagccagag	gttcctccac	aacaaccagt				630

&lt;210&gt; 359

&lt;211&gt; 620

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 359

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ctgtaaaagt	gtgacagtgt					620

&lt;210&gt; 360

&lt;211&gt; 431

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 360

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&lt;210&gt; 361

&lt;211&gt; 351

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 361

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ctgccactct	gtcctccagc	tctgacagct	cctcatctgt	ggtcctgttg	t	351

&lt;210&gt; 362

&lt;211&gt; 463

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 362

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cccgcgtcac	agaaatgacc	aggttgggtg	ttttcagggt	ccagtgtctg	gtcagcagct	180
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cacacttgca	cacattctcc	ctgataagca	cgatggtgtg	gacaggaagg	aaggatttca	420
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&lt;210&gt; 363

&lt;211&gt; 653

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(653)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 363

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&lt;210&gt; 364

&lt;211&gt; 401

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 364

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aagtggtatg	gcggaataatg	aaatcttctt	caatagccca	g		401

&lt;210&gt; 365

&lt;211&gt; 356

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 365

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&lt;210&gt; 366

&lt;211&gt; 1851

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 366

tcataccat	tgccagcagc	ggcaccgtta	gtcaggtttt	ctgggaatcc	cacatgagta	60
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aaggtagtc cttctatgc ctgttttgcg gaggggttta attctctgctg c 1851

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&lt;210&gt; 367

&lt;211&gt; 668

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 367

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aaaaaaa

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&lt;210&gt; 368

&lt;211&gt; 1512

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 368

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&lt;210&gt; 369

&lt;211&gt; 1853

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 369

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&lt;210&gt; 370

&lt;211&gt; 2184

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 370

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<210> 371  
 <211> 1855  
 <212> DNA  
 <213> Homo sapien

<220>  
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<400> 371

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<210> 372  
 <211> 1059  
 <212> DNA  
 <213> Homo sapien

<400> 372

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<210> 373  
 <211> 1155  
 <212> DNA  
 <213> Homo sapien

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<210> 374  
 <211> 2000  
 <212> DNA  
 <213> Homo sapien

<400> 374						
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&lt;210&gt; 375

&lt;211&gt; 2040

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 375

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&lt;210&gt; 376

&lt;211&gt; 329

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 376

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Leu His Leu Ala Gly Ser Asp Leu Leu Ser Arg Ser Leu Met Ala Glu
 20          25          30
Glu Tyr Thr Ile Val His Ala Ser Phe Ile Ser Cys Ile Ser Ser Ser
 35          40          45
Leu Asp Gly Gln Gly Glu Arg Gln Glu Gln Arg Gly His Phe Trp Arg
 50          55          60
Pro Gln Arg Leu Leu Cys Glu Asp Ala Trp Glu Gln Glu Val Gln Val
 65          70          75          80
Val Leu Pro Leu Leu Pro Leu Leu Gln Gly Ser Gly Lys Ser Asn Val
 85          90          95
Val Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe Met Asp Pro Arg Tyr
100          105          110
His Val His Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp
115          120          125
Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp
130          135          140
Val Asn Lys Arg Asp Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser
145          150          155          160
Ala Asn Gly Asn Ser Glu Val Val Lys Leu Val Leu Asp Arg Arg Cys
165          170          175
Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala
180          185          190
Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly
195          200          205
Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr
210          215          220
Ala Val Tyr Asn Glu Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr
225          230          235          240
Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu
245          250          255
Leu Gly Ile His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys
260          265          270
Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu
275          280          285
Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu

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290 295 300  
 Glu Gln Asn Val Asp Val Ser Ser Gln Asp Leu Glu Arg Arg Pro Glu  
 305 310 315 320  
 Ser Met Leu Phe Leu Val Ile Ile Met  
 325

<210> 377  
 <211> 148  
 <212> PRT  
 <213> Homo sapien

<220>  
 <221> VARIANT  
 <222> (1)...(148)  
 <223> Xaa = Any Amino Acid

<400> 377  
 Met Thr Xaa Pro Ser Trp Ser Pro Gly Thr Thr Ser Val Glu Lys Ile  
 1 5 10 15  
 Trp Thr Ser Ser Thr Glu Leu Pro Trp Trp Gly Lys Val Pro Arg Lys  
 20 25 30  
 Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Xaa Asp Lys  
 35 40 45  
 Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu  
 50 55 60  
 Val Val Lys Leu Xaa Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp  
 65 70 75 80  
 Asn Lys Lys Arg Thr Ala Leu Xaa Lys Ala Val Gln Cys Gln Glu Asp  
 85 90 95  
 Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro  
 100 105 110  
 Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Xaa Tyr Asn Glu Asp  
 115 120 125  
 Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser  
 130 135 140  
 Lys Asn Lys Val  
 145

<210> 378  
 <211> 1719  
 <212> PRT  
 <213> Homo sapien

<400> 378  
 Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys  
 1 5 10 15  
 Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe  
 20 25 30  
 Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp  
 35 40 45  
 His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp  
 50 55 60  
 Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val  
 65 70 75 80  
 Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn

					85					90					95		
Lys	Met	Gly	Lys	Trp	Cys	Cys	His	Cys	Phe	Pro	Cys	Cys	Arg	Gly	Ser		
			100					105					110				
Gly	Lys	Ser	Lys	Val	Gly	Ala	Trp	Gly	Asp	Tyr	Asp	Asp	Ser	Ala	Phe		
			115				120					125					
Met	Glu	Pro	Arg	Tyr	His	Val	Arg	Gly	Glu	Asp	Leu	Asp	Lys	Leu	His		
			130			135					140						
Arg	Ala	Ala	Trp	Trp	Gly	Lys	Val	Pro	Arg	Lys	Asp	Leu	Ile	Val	Met		
					150					155					160		
Leu	Arg	Asp	Thr	Asp	Val	Asn	Lys	Lys	Asp	Lys	Gln	Lys	Arg	Thr	Ala		
				165					170					175			
Leu	His	Leu	Ala	Ser	Ala	Asn	Gly	Asn	Ser	Glu	Val	Val	Lys	Leu	Leu		
			180					185					190				
Leu	Asp	Arg	Arg	Cys	Gln	Leu	Asn	Val	Leu	Asp	Asn	Lys	Lys	Arg	Thr		
			195				200					205					
Ala	Leu	Ile	Lys	Ala	Val	Gln	Cys	Gln	Glu	Asp	Glu	Cys	Ala	Leu	Met		
			210			215					220						
Leu	Leu	Glu	His	Gly	Thr	Asp	Pro	Asn	Ile	Pro	Asp	Glu	Tyr	Gly	Asn		
				230						235				240			
Thr	Thr	Leu	His	Tyr	Ala	Ile	Tyr	Asn	Glu	Asp	Lys	Leu	Met	Ala	Lys		
			245					250					255				
Ala	Leu	Leu	Leu	Tyr	Gly	Ala	Asp	Ile	Glu	Ser	Lys	Asn	Lys	His	Gly		
			260				265					270					
Leu	Thr	Pro	Leu	Leu	Leu	Gly	Val	His	Glu	Gln	Lys	Gln	Gln	Val	Val		
			275				280					285					
Lys	Phe	Leu	Ile	Lys	Lys	Lys	Ala	Asn	Leu	Asn	Ala	Leu	Asp	Arg	Tyr		
				295							300						
Gly	Arg	Thr	Ala	Leu	Ile	Leu	Ala	Val	Cys	Cys	Gly	Ser	Ala	Ser	Ile		
			310					315						320			
Val	Ser	Leu	Leu	Leu	Glu	Gln	Asn	Ile	Asp	Val	Ser	Ser	Gln	Asp	Leu		
			325					330					335				
Ser	Gly	Gln	Thr	Ala	Arg	Glu	Tyr	Ala	Val	Ser	Ser	His	His	His	Val		
			340				345					350					
Ile	Cys	Gln	Leu	Leu	Ser	Asp	Tyr	Lys	Glu	Lys	Gln	Met	Leu	Lys	Ile		
			355				360					365					
Ser	Ser	Glu	Asn	Ser	Asn	Pro	Glu	Asn	Val	Ser	Arg	Thr	Arg	Asn	Lys		
			370			375					380						
Pro	Arg	Thr	His	Met	Val	Val	Glu	Val	Asp	Ser	Met	Pro	Ala	Ala	Ser		
			385		390				395					400			
Ser	Val	Lys	Lys	Pro	Phe	Gly	Leu	Arg	Ser	Lys	Met	Gly	Lys	Trp	Cys		
			405					410				415					

Asp Lys Leu His Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp  
 530 535 540  
 Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln  
 545 550 555 560  
 Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val  
 565 570 575  
 Val Lys Leu Leu Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn  
 580 585 590  
 Lys Lys Arg Thr Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu  
 595 600 605  
 Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp  
 610 615 620  
 Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys  
 625 630 635 640  
 Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys  
 645 650 655  
 Asn Lys His Gly Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys  
 660 665 670  
 Gln Gln Val Val Lys Phe Leu Ile Lys Lys Ala Asn Leu Asn Ala  
 675 680 685  
 Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly  
 690 695 700  
 Ser Ala Ser Ile Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser  
 705 710 715 720  
 Ser Gln Asp Leu Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser  
 725 730 735  
 His His His Val Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln  
 740 745 750  
 Met Leu Lys Ile Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys  
 755 760 765  
 Leu Thr Ser Glu Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser  
 770 775 780  
 Gln Pro Glu Lys Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp  
 785 790 795 800  
 Arg Glu Val Glu Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly  
 805 810 815  
 Leu Leu Glu Asn Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn  
 820 825 830  
 Gly Leu Ile Pro Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe  
 835 840 845  
 Pro Asp Asn Glu Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser  
 850 855 860  
 Asp Tyr Lys Glu Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn  
 865 870 875 880  
 Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu Glu Ser Gln Arg Leu  
 885 890 895  
 Glu Gly Ser Glu Asn Gly Gln Pro Glu Leu Glu Asn Phe Met Ala Ile  
 900 905 910  
 Glu Glu Met Lys Lys His Gly Ser Thr His Val Gly Phe Pro Glu Asn  
 915 920 925  
 Leu Thr Asn Gly Ala Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro  
 930 935 940  
 Pro Arg Lys Ser Arg Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu  
 945 950 955 960  
 Asn Glu Glu Tyr His Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe

965 970 975  
 Cys Glu Glu Gln Asn Thr Gly Ile Leu His Asp Glu Ile Leu Ile His  
 980 985 990  
 Glu Glu Lys Gln Ile Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser  
 995 1000 1005  
 Leu Ser Cys Lys Lys Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu  
 1010 1015 1020  
 Arg Glu Glu Ile Ala Met Leu Arg Leu Glu Leu Asp Thr Met Lys His  
 1025 1030 1035 104  
 Gln Ser Gln Leu Pro Arg Thr His Met Val Val Glu Val Asp Ser Met  
 1045 1050 1055  
 Pro Ala Ala Ser Ser Val Lys Lys Pro Phe Gly Leu Arg Ser Lys Met  
 1060 1065 1070  
 Gly Lys Trp Cys Cys Arg Cys Phe Pro Cys Cys Arg Glu Ser Gly Lys  
 1075 1080 1085  
 Ser Asn Val Gly Thr Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr  
 1090 1095 1100  
 Leu Arg Ser Lys Met Gly Lys Trp Cys Arg His Cys Phe Pro Cys Cys  
 1105 1110 1115 112  
 Arg Gly Ser Gly Lys Ser Asn Val Gly Ala Ser Gly Asp His Asp Asp  
 1125 1130 1135  
 Ser Ala Met Lys Thr Leu Arg Asn Lys Met Gly Lys Trp Cys Cys His  
 1140 1145 1150  
 Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Lys Val Gly Ala Trp  
 1155 1160 1165  
 Gly Asp Tyr Asp Asp Ser Ala Phe Met Glu Pro Arg Tyr His Val Arg  
 1170 1175 1180  
 Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp Gly Lys Val  
 1185 1190 1195 120  
 Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys  
 1205 1210 1215  
 Lys Asp Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly  
 1220 1225 1230  
 Asn Ser Glu Val Val Lys Leu Leu Leu Asp Arg Arg Cys Gln Leu Asn  
 1235 1240 1245  
 Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Ile Lys Ala Val Gln Cys  
 1250 1255 1260  
 Gln Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro  
 1265 1270 1275 128  
 Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Ile Tyr  
 1285 1290 1295  
 Asn Glu Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp  
 1300 1305 1310  
 Ile Glu Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu Leu Gly Val  
 1315 1320 1325  
 His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala  
 1330 1335 1340  
 Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala  
 1345 1350 1355 136  
 Val Cys Cys Gly Ser Ala Ser Ile Val Ser Leu Leu Glu Gln Asn  
 1365 1370 1375  
 Ile Asp Val Ser Ser Gln Asp Leu Ser Gly Gln Thr Ala Arg Glu Tyr  
 1380 1385 1390  
 Ala Val Ser Ser His His His Val Ile Cys Gln Leu Leu Ser Asp Tyr  
 1395 1400 1405



Lys Glu Lys Gln Met Leu Lys Ile Ser Ser Glu Asn Ser Asn Pro Glu  
 1410 1415 1420  
 Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Phe Lys Gly  
 1425 1430 1435 144  
 Ser Glu Asn Ser Gln Pro Glu Lys Met Ser Gln Glu Pro Glu Ile Asn  
 1445 1450 1455  
 Lys Asp Gly Asp Arg Glu Val Glu Glu Glu Met Lys Lys His Glu Ser  
 1460 1465 1470  
 Asn Asn Val Gly Leu Leu Glu Asn Leu Thr Asn Gly Val Thr Ala Gly  
 1475 1480 1485  
 Asn Gly Asp Asn Gly Leu Ile Pro Gln Arg Lys Ser Arg Thr Pro Glu  
 1490 1495 1500  
 Asn Gln Gln Phe Pro Asp Asn Glu Ser Glu Glu Tyr His Arg Ile Cys  
 1505 1510 1515 152  
 Glu Leu Val Ser Asp Tyr Lys Glu Lys Gln Met Pro Lys Tyr Ser Ser  
 1525 1530 1535  
 Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu  
 1540 1545 1550  
 Ser Gln Arg Leu Glu Gly Ser Glu Asn Gly Gln Pro Glu Lys Arg Ser  
 1555 1560 1565  
 Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Leu Glu Asn Phe  
 1570 1575 1580  
 Met Ala Ile Glu Glu Met Lys Lys His Gly Ser Thr His Val Gly Phe  
 1585 1590 1595 160  
 Pro Glu Asn Leu Thr Asn Gly Ala Thr Ala Gly Asn Gly Asp Asp Gly  
 1605 1610 1615  
 Leu Ile Pro Pro Arg Lys Ser Arg Thr Pro Glu Ser Gln Gln Phe Pro  
 1620 1625 1630  
 Asp Thr Glu Asn Glu Glu Tyr His Ser Asp Glu Gln Asn Asp Thr Gln  
 1635 1640 1645  
 Lys Gln Phe Cys Glu Glu Gln Asn Thr Gly Ile Leu His Asp Glu Ile  
 1650 1655 1660  
 Leu Ile His Glu Glu Lys Gln Ile Glu Val Val Glu Lys Met Asn Ser  
 1665 1670 1675 168  
 Glu Leu Ser Leu Ser Cys Lys Lys Glu Lys Asp Ile Leu His Glu Asn  
 1685 1690 1695  
 Ser Thr Leu Arg Glu Glu Ile Ala Met Leu Arg Leu Glu Leu Asp Thr  
 1700 1705 1710  
 Met Lys His Gln Ser Gln Leu  
 1715

&lt;210&gt; 379

&lt;211&gt; 656

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 379

Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys  
 1 5 10 15  
 Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe  
 20 25 30  
 Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp  
 35 40 45  
 His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp  
 50 55 60

Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val  
 65 70 75 80  
 Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn  
 85 90 95  
 Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser  
 100 105 110  
 Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe  
 115 120 125  
 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His  
 130 135 140  
 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met  
 145 150 155 160  
 Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala  
 165 170 175  
 Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu  
 180 185 190  
 Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr  
 195 200 205  
 Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met  
 210 215 220  
 Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn  
 225 230 235 240  
 Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys  
 245 250 255  
 Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly  
 260 265 270  
 Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val  
 275 280 285  
 Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr  
 290 295 300  
 Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile  
 305 310 315 320  
 Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu  
 325 330 335  
 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His His Val  
 340 345 350  
 Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu Lys Ile  
 355 360 365  
 Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu  
 370 375 380  
 Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser Gln Pro Glu Lys  
 385 390 395 400  
 Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Val Glu  
 405 410 415  
 Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly Leu Leu Glu Asn  
 420 425 430  
 Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn Gly Leu Ile Pro  
 435 440 445  
 Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe Pro Asp Asn Glu  
 450 455 460  
 Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser Asp Tyr Lys Glu  
 465 470 475 480  
 Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp  
 485 490 495  
 Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu Glu Gly Ser Glu

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      500                      505                      510
Asn Gly Gln Pro Glu Leu Glu Asn Phe Met Ala Ile Glu Glu Met Lys
      515                      520                      525
Lys His Gly Ser Thr His Val Gly Phe Pro Glu Asn Leu Thr Asn Gly
      530                      535                      540
Ala Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro Pro Arg Lys Ser
545                      550                      555                      560
Arg Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu Asn Glu Glu Tyr
      565                      570                      575
His Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe Cys Glu Glu Gln
      580                      585                      590
Asn Thr Gly Ile Leu His Asp Glu Ile Leu Ile His Glu Glu Lys Gln
      595                      600                      605
Ile Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser Leu Ser Cys Lys
610                      615                      620
Lys Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu Arg Glu Glu Ile
625                      630                      635                      640
Ala Met Leu Arg Leu Glu Leu Asp Thr Met Lys His Gln Ser Gln Leu
      645                      650                      655

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&lt;210&gt; 380

&lt;211&gt; 671

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 380

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Met Val Val Glu Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys
  1                      5                      10                      15
Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe
      20                      25                      30
Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp
      35                      40                      45
His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp
50                      55                      60
Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val
65                      70                      75                      80
Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn
      85                      90                      95
Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser
      100                      105                      110
Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe
      115                      120                      125
Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His
      130                      135                      140
Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met
145                      150                      155                      160
Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala
      165                      170                      175
Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu
      180                      185                      190
Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr
      195                      200                      205
Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met
210                      215                      220
Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn

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225					230					235						240
Thr	Thr	Leu	His	Tyr	Ala	Ile	Tyr	Asn	Glu	Asp	Lys	Leu	Met	Ala	Lys	
				245					250					255		
Ala	Leu	Leu	Leu	Tyr	Gly	Ala	Asp	Ile	Glu	Ser	Lys	Asn	Lys	His	Gly	
				260					265					270		
Leu	Thr	Pro	Leu	Leu	Leu	Gly	Val	His	Glu	Gln	Lys	Gln	Gln	Val	Val	
				275					280					285		
Lys	Phe	Leu	Ile	Lys	Lys	Lys	Ala	Asn	Leu	Asn	Ala	Leu	Asp	Arg	Tyr	
				290					295					300		
Gly	Arg	Thr	Ala	Leu	Ile	Leu	Ala	Val	Cys	Cys	Gly	Ser	Ala	Ser	Ile	
305					310						315				320	
Val	Ser	Leu	Leu	Leu	Glu	Gln	Asn	Ile	Asp	Val	Ser	Ser	Gln	Asp	Leu	
				325					330					335		
Ser	Gly	Gln	Thr	Ala	Arg	Glu	Tyr	Ala	Val	Ser	Ser	His	His	His	Val	
				340					345					350		
Ile	Cys	Gln	Leu	Leu	Ser	Asp	Tyr	Lys	Glu	Lys	Gln	Met	Leu	Lys	Ile	
				355					360					365		
Ser	Ser	Glu	Asn	Ser	Asn	Pro	Glu	Gln	Asp	Leu	Lys	Leu	Thr	Ser	Glu	
				370								380				
Glu	Glu	Ser	Gln	Arg	Phe	Lys	Gly	Ser	Glu	Asn	Ser	Gln	Pro	Glu	Lys	
385					390						395				400	
Met	Ser	Gln	Glu	Pro	Glu	Ile	Asn	Lys	Asp	Gly	Asp	Arg	Glu	Val	Glu	
				405							410			415		
Glu	Glu	Met	Lys	Lys	His	Glu	Ser	Asn	Asn	Val	Gly	Leu	Leu	Glu	Asn	
				420					425					430		
Leu	Thr	Asn	Gly	Val	Thr	Ala	Gly	Asn	Gly	Asp	Asn	Gly	Leu	Ile	Pro	
				435					440					445		
Gln	Arg	Lys	Ser	Arg	Thr	Pro	Glu	Asn	Gln	Gln	Phe	Pro	Asp	Asn	Glu	
				450								460				
Ser	Glu	Glu	Tyr	His	Arg	Ile	Cys	Glu	Leu	Val	Ser	Asp	Tyr	Lys	Glu	
465					470						475				480	
Lys	Gln	Met	Pro	Lys	Tyr	Ser	Ser	Glu	Asn	Ser	Asn	Pro	Glu	Gln	Asp	
				485							490			495		
Leu	Lys	Leu	Thr	Ser	Glu	Glu	Glu	Ser	Gln	Arg	Leu	Glu	Gly	Ser	Glu	
				500					505					510		
Asn	Gly	Gln	Pro	Glu	Lys	Arg	Ser	Gln	Glu	Pro	Glu	Ile	Asn	Lys	Asp	
				515					520					525		
Gly	Asp	Arg	Glu	Leu	Glu	Asn	Phe	Met	Ala	Ile	Glu	Glu	Met	Lys	Lys	
				530								540				
His	Gly	Ser	Thr	His	Val	Gly	Phe	Pro	Glu	Asn	Leu	Thr	Asn	Gly	Ala	
545					550						555				560	
Thr	Ala	Gly	Asn	Gly	Asp	Asp	Gly	Leu	Ile	Pro	Pro	Arg	Lys	Ser	Arg	
				565					570							

<210> 381  
<211> 251  
<212> DNA  
<213> Homo sapien

<400> 381

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ggtaacatgc	ttcccctaag	ggtatcccaa	cccagggggc	tcaccatgac	ctctgagggg	120
ccaatatccc	aggagaagca	ttggggagtt	gggggcaggt	gaaggaccca	ggactcacac	180
atcctggggc	tccaaggcag	aggagagggg	cctcaagaag	gtcaggagga	aaatccgtaa	240
caagcagtca	g					251

<210> 382  
<211> 3279  
<212> DNA  
<213> Homo sapiens

<400> 382

cttcctgcag	cccccatgct	ggtgaggggc	acgggcagga	acagtggacc	caacatggaa	60
atgctggagg	gtgtcaggaa	gtgatcgggc	tctggggcag	ggaggagggg	tggggagtgt	120
cactggggag	ggacatcctg	cagaaggtag	gagtgcagaa	acaccgcctg	caggggaggg	180
gagagccctg	cggcacctgg	gggagcagag	ggagcagcac	ctgcccagcg	ctgggaggag	240
gggctggag	ggcgtgagga	ggagcagggg	ggctgcattg	ctggagttag	ggatcagggg	300
cagggcgcca	gatggcctca	cacaggggag	agagggcccc	tcctgcaggg	cctcacctgg	360
gccacaggag	gacactgctt	ttcctctgag	gagtcaggag	ctgtggatgg	tgtctggacag	420
aagaaggaca	gggcttgctc	caggtgtcca	gaggctgtcg	ctggcttccc	tttgggatca	480
gactgcaggg	agggaggggc	gcagggttgt	ggggggagtg	acgatgagga	tgacctgggg	540
gtggctccag	gccttgcccc	tgctggggcc	ctcacccagc	ctccctcaca	gtctctctgg	600
cctcagttct	tcctctccac	tcctcctctc	atctggcctc	agtggttcct	tctgatcact	660
gaactgacca	taccagcccc	tgccccagcg	cctccatggc	tccccaatgc	cctggagagg	720
ggacatctag	tcagagagta	gtcctgaaga	ggtaggctct	gcgatgtgcc	tgtgggggca	780
gcactctcca	gatggctccc	ggcctcatcc	tgctgacctg	tctgcaggga	gtctctctct	840
ggaccttgcc	ccttgtgcag	gagctggacc	ctgaagctcc	ctccccatag	gcctcagagt	900
gagccttgtt	ccctctgttg	gactccctgc	ccatattctt	gtgggagtgg	gttctggaga	960
cattttctgt	tgcttctgag	agctgggaat	tgctctcagt	catctgcctg	cgcgggttct	1020
agagatggag	ttgcctaggc	agttattggg	gccaatcttt	ctcactgtgt	ctctctctct	1080
ttacccttag	ggtgattctg	ggggctccat	tgctgtgaat	ggtgtgcttc	aaggatcac	1140
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tgtttgtggg	gtgcagagat	gggaggggtg	ggggccaccc	tgggaagagt	gacagtgaca	1620
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taggggggag	aactgaaagc	tgatttaatta	caggaggttt	gttcaggttcc	cccaaaccac	1860
cgtcagattt	gatgatttcc	tcagcaggact	tacagaaata	aagagctatc	atgctgtggg	1920
ttattatggt	ttgttacatt	gataggatac	atactgaaat	cagcaaacaa	aacagatgta	1980
tagattagag	tggtggagaaa	acagaggaaa	acttgcagtt	acgaagactg	gcaacttggc	2040
tttactaagt	tttcagactg	gcaggaagtc	aaacctatta	ggctgaggag	cttgtggagt	2100
gtagctgatc	cagctgatag	aggaaactagc	caggtggggg	cctttccctt	tggatggggg	2160

```

gcatatccga cagttattct ctccaagtgg agacttacgg acagcatata attctccctg 2220
caaggatgta tgataatatg tacaaaagtaa ttccaactga ggaagctcac ctgaccccta 2280
gtgtccaggg tttttactgg ggggtctgtag gacgagtatg gagtacttga ataattgacc 2340
tgaagtccctc agacctgagg ttccctagag ttcaaacaga tacagcatgg tccagagtcc 2400
cagatgtaca aaaacaggga ttcatcacia atcccatctt tagcatgaag ggtctggcat 2460
ggcccaaggc cccaagtata tcaaggcact tgggcagaac atgccaaagga atcaaatgtc 2520
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gcagggtctg tagtcaacc ttttattgta caggggatga gggaaaggga gaggatgagg 2640
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atcattgttt tatttgcctt cttttcacac cattgggtgag ggagggatta ccaccttggg 2820
gttatgaaga tggttgaaca cccacacat agcaccggag atatgagatc aacagtttct 2880
tagccataga gattcacagc ccagagcagg aggacgctgc acaccatgca ggatgacatg 2940
ggggatgcgc tcgggattgg tgtgaagaag caaggactgt tagaggcagg ctttatagta 3000
acaagacggt ggggcaaac ctgatttccg tgggggaatg tcatgggtct gctttactaa 3060
gttttgagac tggcaggtag tgaaactcat taggctgaga accttgtgga atgcagctga 3120
cccagctgat agaggaagta gccagggtggg agcctttccc agtggggtgtg ggacatatct 3180
ggcaagattt tgtggcactc ctggttacag atactggggc agcaataaaa actgaatctt 3240
gttttcagac cttaaaaaaa aaaaaaaaaa aaaagtttt 3279

```

&lt;210&gt; 383

&lt;211&gt; 155

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 383

```

Met Ala Gly Val Arg Asp Gln Gly Gln Gly Ala Arg Trp Pro His Thr
                5                                10                    15

```

```

Gly Lys Arg Gly Pro Leu Leu Gln Gly Leu Thr Trp Ala Thr Gly Gly
                20                                25                    30

```

```

His Cys Phe Ser Ser Glu Glu Ser Gly Ala Val Asp Gly Ala Gly Gln
                35                                40                    45

```

```

Lys Lys Asp Arg Ala Trp Leu Arg Cys Pro Glu Ala Val Ala Gly Phe
                50                                55                    60

```

```

Pro Leu Gly Ser Asp Cys Arg Glu Gly Gly Arg Gln Gly Cys Gly Gly
                65                                70                    75                    80

```

```

Ser Asp Asp Glu Asp Asp Leu Gly Val Ala Pro Gly Leu Ala Pro Ala
                85                                90                    95

```

```

Trp Ala Leu Thr Gln Pro Pro Ser Gln Ser Pro Gly Pro Gln Ser Leu
                100                               105                    110

```

```

Pro Ser Thr Pro Ser Ser Ile Trp Pro Gln Trp Val Ile Leu Ile Thr
                115                               120                    125

```

```

Glu Leu Thr Ile Pro Ser Pro Ala His Gly Pro Pro Trp Leu Pro Asn
                130                               135                    140

```

```

Ala Leu Glu Arg Gly His Leu Val Arg Glu
                145                               150

```

<210> 384  
<211> 557  
<212> DNA  
<213> Homo sapiens

<400> 384  
ggatcctcta gagcgccgc ctactactac taaattcgcg gccgcgtcga cgaagaagag 60  
aaagatgtgt tttgttttg actctctgtg gtcccttcca atgctgtggg ttccaacca 120  
ggggaagggt cccttttgca ttgccaagt ccataaccat gagcactact ctaccatggt 180  
tctgcctcct ggccaagcag gctggtttgc aagaatgaaa tgaatgatc tacagctagg 240  
acttaacctt gaaatggaaa gtcttgcaat ccatttgca ggatccgtct gtgcacatgc 300  
ctctgtagag agcagcattc ccagggaacct tggaaacagt tggcactgta aggtgcttgc 360  
tccccaagac acatcctaaa aggtgttgta atggtgaaaa cgtcttcctt ctttattgcc 420  
ccttcttatt tatgtgaaca actgtttgtc tttttttgta tcttttttaa actgtaaagt 480  
tcaattgtga aaatgaatat catgcaaata aattatgcga ttttttttc aaagtaaaaa 540  
aaaaaaaa aaaaaaa 557

<210> 385  
<211> 337  
<212> DNA  
<213> Homo sapiens

<400> 385  
ttcccagggt atgtgcgagg gaagacacat ttactatcct tgatggggct gattccttta 60  
gtttctctag cagcagatgg gttaggagga agtgacccaa gtggttgact cctatgtgca 120  
tctcaaagcc atctgtctgtc ttccagtagc gacacatcat cactcctgca ttgttgatca 180  
aaacgtggag gtgcttttcc tcagctaaga agcccttagc aaaagctcga atagacctag 240  
tatcagacag gtccagtttc cgcaccaaca cctgctggtt cctgtcgtg gtctggtatc 300  
ctttggccac caattccccc ttttccacat cccggca 337

<210> 386  
<211> 300  
<212> DNA  
<213> Homo sapiens

<400> 386  
gggcccgtca ccggcccagg ccccgccctc cgagtcctcc tccccgggtg cctgcccgcga 60  
gcccgctcgg ccagagagggt gggcgccggg ctgcctctac cggctggcgg ctgtaactca 120  
gcgaccttgg ccgaagggt ctagcaagga ccaccgacc ccagccggc cggcgccggc 180  
gcggactttg cccggtgtgt ggggcggagc ggactgctg tcccgggacg ggcagcgaag 240  
atgttagcct tcgctgccag gaccgtggac cgatcccagg gctgtggtgt aacctcagcc 300

<210> 387  
<211> 537  
<212> DNA  
<213> Homo sapiens

<400> 387  
gggcccagtc gggcaccaag ggactctttg caggcttctt tcctcggtac atcaaggctg 60  
ccccctctct tgccatcatg atcagcactt atgagttcgg caaaagcttc ttccagaggc 120  
tgaaccagga ccggtctctg ggcggctgaa aggggcaagg aggcaggac ccgctctctc 180  
ccacggatgg ggagagggca ggaggagacc cagccaagtg ccttttctc agcactgagg 240  
gagggggcct gtttcccttc cctcccgccg acaagctcca gggcagggct gtccctctgg 300

```

gcggcccagc acttcctcag acacaacttc ttcttgctgc tccagtcgtg gggatcatca 360
cttaccaccacc ccccaagttc aagaccaaat ctccagctg ccccttcgtg gtttccctgt 420
gtttgctgta gctgggcatg tctccaggaa ccaagaagcc ctacgctgg tgtagtctcc 480
ctgacccttg ttaattcctt aagtctaaag atgatgaact tcaaaaaaaa aaaaaaa 537

```

<210> 388

<211> 520

<212> DNA

<213> Homo sapiens

<400> 388

```

aggataattt ttaaaccaat caaatgaaaa aaacaaacaa aaaaaaaagg aaatgtcatg 60
tgagggttaaa ccagtttgca ttcccctaata gtggaaaaag taagaggact actcagcact 120
gtttgaagat tgccctttct acagcttctg agaattgtgt tatttcactt gccaaagtga 180
ggacccccctc cccaacatgc ccagagccac ccctaagcat ggctccctgt caccaggcaa 240
ccaggaaact gctactttgt gacctcacca gagaccagga ggggtttggtt agctcacagg 300
acttccccca cccagaaga ttagcatccc atactagact cataactcaa tcaactaggc 360
tcataactcaa ttgatgggta ttagacaatt ccatttcttt ctgggttatta taaacagaaa 420
atctttcctc ttctcattac cagtaaaggc tcttggtatc tttctgttgg aatgatttct 480
atgaacttgt cttattttaa tgggtgggtt ttttctcgtt 520

```

<210> 389

<211> 365

<212> DNA

<213> Homo sapiens

<400> 389

```

cgttgcacca gtttgacaga aggaaaggcg gagcttattc aaagtcctaga gggagtgagg 60
gagttaaggc tggatttcag atctgcctgg ttccagccgc agtggtgccct ctgctcccc 120
aacgactttc caaataatct caccagcgcc ttccagctca ggcgtcctag aagcgtcttg 180
aagcctatgg ccagctgtct ttgtgtccc tctcacccgc ctgctcctac agctgagact 240
cccaggaaac ctctcagacta ccttcctctg ccttcagcaa ggggcgttgc ccacattctc 300
tgagggtcag tggaagaacc tagactccca ttgctagagg tagaaagggg aagggtgctg 360
gggag 365

```

<210> 390

<211> 221

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(221)

<223> n = A,T,C or G

<400> 390

```

tgctctccca tcctggcccc gacttctctg tcaggaaagt ggggatggac cccatctgca 60
tacacggntt ctcatgggtg tggaacatct ctgcttgctg ttccaggaaag gcctctggct 120
gctctangag tctgancnga ntcgttgccc cantntgaca naaggaaagg cggagcttat 180
tcaaagtcta gagggagtgg agggagttaag gctggatttc a 221

```

<210> 391

<211> 325

<212> DNA

<213> Homo sapiens



&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(325)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 391

```

tggagcaggt cccgaggcct ccctagagcc tggggccgac tctgtgncga tgcangcttt 60
ctctcgcgcc cagcctggag ctgctcctgg catctaccaa caatcagncg aggcgagcag 120
tagccagggc actgctgcca acagccagtc cnnataccat catgtnaccc ggtgngctct 180
naantngat ntccanagcc ctacccatcn tagttctgct ctcccaccgg ntaccagccc 240
cactgcccag gaactctaca gccagtaccc tgtcccgcag tctctaccta ccagtacgat 300
gagacctccg gctactacta tgacc
325

```

&lt;210&gt; 392

&lt;211&gt; 277

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(277)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 392

```

atattgttta actccttcct ttatatcttt taacattttc atggngaaag gttcacatct 60
agttctactt nggcagnagn ctctacttg agtctcttcc ccggcctggn ccagtnagna 120
antaccanga accgncatgn cttanaaacn ncctggtttn tgggttnntc aatgactgca 180
tgcagtgcac caccctgtcc actacgtgat gctgtaggat taaagtctca cagtgggcgy 240
ctgaggatac agcgcgcgct cctgtgttgc tggggaa
277

```

&lt;210&gt; 393

&lt;211&gt; 566

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 393

```

actagtcag tgtggtggaa ttcgcgccg cgtcgacgga caggtcagct gcttggtca 60
gtgatctaca ttctgaagtt gtctgaaat gtcttcatga ttaaatcag cctaaacgtt 120
ttgccgggaa cactgcagag acaatgctgt gagtttccaa ccttagccca tctgcgggca 180
gagaaggctc agtttgtcca tcagcattat catgatatca ggactgggta cttggttaag 240
gaggggtcta ggagatctgt cccttttaga gacaccttac ttataatgaa gtatttggga 300
gggtgggttt caaaagtaga aatgtcctgt attccgatga tcatcctgta aacattttat 360
catttattaa tcatccctgc ctgtgtctat tattatattc atatctctac gctggaaact 420
ttctgcctca atgtttactg tgcccttgtt ttgtctagtt tgtgtgtgtt aaaaaaaaaa 480
cattctctgc ctgagtttta attttgttcc aaagtatttt taatctatac aattaaaagc 540
ttttgcctat caaaaaaaaa aaaaaa
566

```

&lt;210&gt; 394

&lt;211&gt; 384

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

<222> (1)...(384)

<223> n = A,T,C or G

<400> 394

```
gaacatacat gtcccggcac ctgagctgca gtctgacatc atcgccatca cgggcctcgc 60
tgcaaatnng gaccgggcca aggctggact gctggagcgt gtgaaggagc tacaggccna 120
gcaggaggac cgggctttaa ggagttttaa gctgagtgtc actgtagacc ccaaatacca 180
tcccaagatt atcgggagaa agggggcagt aattacccaa atccggttgg agcatgacgt 240
gaacatccag ttccctgata aggacgatgg gaaccagccc caggacacaa ttaccatcac 300
agggtacgaa aagaacacag aagctgccag ggatgctata ctgagaattg tgggtgaact 360
tgagcagatg gtttctgagg acgt                                     384
```

<210> 395

<211> 399

<212> DNA

<213> Homo sapiens

<400> 395

```
ggcaaaactg tgtgacctca ataagacctc gcagatccaa ggtcaagtat cagaagtgc 60
tctgaccttg gactccaaga cctacatcaa cagcctggct atattagatg atgagccagt 120
tatcagaggt ttcatcattg cggaaattgt ggagtctaag gaaatcatgg cctctgaagt 180
attcacgtct ttccagtacc ctgagttctc tatagagttg cctaacacag gcagaattgg 240
ccagctactt gtctgcaatt gtatcttcaa gaataccctg gccatccctt tgactgacgt 300
caagttctct ttggaaagcc tgggcatctc ctcactacag acctctgacc atgggacggg 360
gcagcctggg gagaccatcc aatcccaaat aaaatgcac                                     399
```

<210> 396

<211> 403

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(403)

<223> n = A,T,C or G

<400> 396

```
tggagtnttc agtgcaaaac agccataaag cttcagtagc aaattactgt ctcacagaaa 60
gacattttca acttctgctc cagctgctga taaaacaaat catgtgttta gcttgactcc 120
agacaaggac aacctgttcc ttcataactc tctagagaaa aaaaggagtt gttagtagat 180
actaaaaaaa gtggatgaat aatctggata tttttcctaa aaagattcct tgaaacacat 240
taggaaaaatg gagggcctta tgatcagaat gctagaatta gtccattgtg ctgaagcagg 300
gttttagggga gggagtggag gataaaagaa ggaaaaaaag aagagtgaga aaacctatct 360
atcaaagcag gtgctatcac tcaatgttag gccctgctct ttt                                     403
```

<210> 397

<211> 100

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(100)

<223> n = A,T,C or G

<400> 397  
 actagtnacg tgtggtggaa ttcgcgccg cgtcgacctt naanccatct ctatagcaaa 60  
 tccatccccg ctccctggtg gtnacagaat gactgacaaa 100

<210> 398  
 <211> 278  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(278)  
 <223> n = A,T,C or G

<400> 398  
 gcggccgcgt cgacagcagt tccgccagcg ctgcgccctg ggtggggatg tgctgcacgc 60  
 ccacctggac atctggaagt cagcggcctg gatgaaagag cggacttcac ctggggcgat 120  
 tcaactactgt gcctcgacca gtgaggagag ctggaccgac agcgagggtg actcatcatg 180  
 ctccgggcag cccatccacc tgtggcagtt cctcaaggag ttgctactca agccccacag 240  
 ctatggccgc ttcatnangt ggctcaacaa ggagaagg 278

<210> 399  
 <211> 298  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(298)  
 <223> n = A,T,C or G

<400> 399  
 acggaggtgg aggaagcgc cctgggatcg anaggatggg tcctgncatt gaccncctcn 60  
 ggggtgcnng catggagcgc atgggcgcgg gcctgggcca cggcatggat cgcgtgggct 120  
 ccgagatcga gcgcattggg ctggctcatgg accgcatggg ctccgtggag cgcattgggct 180  
 ccggcattga gcgcattggg ccgctgggcc tcgaccacat ggcctccanc attgancgca 240  
 tgggccagac catggagcgc attggctctg gcgtggagcn catgggtgcc ggcattggg 298

<210> 400  
 <211> 548  
 <212> DNA  
 <213> Homo sapiens

<400> 400  
 acatcaacta cttectcatt ttaaggtatg gcagttccct tcataccctt ttcctgcctt 60  
 gtacatgtac atgtatgaaa ttctcttctc ttaccgaact ctctccacac atcacaagg 120  
 caaagaacca cacgcttaga agggtaagag ggcaccctat gaaatgaaat ggtgatttct 180  
 tgagttctct ttttccacgt ttaaggggccc atggcaggac tttagagttgc gagttaagac 240  
 tgcagagggc tagagaatta ttccatacac gctttgaggc caccatgtc acttatcccg 300  
 tataccctct caccatcccc ttgtctactc tgatgcccc aagatgcaac tgggcagcta 360  
 gttggcccca taattctggg cctttgttgt ttgttttaac tacttgggca tcccaggaag 420  
 ctttccagtg atctcctacc atgggcccc ctccctggat caagccctc ccaggccctg 480  
 tccccagccc ctccctgccc agccccccc cttgccttgg tgctcagccc tccatttggg 540  
 agcaggtt 548

<210> 401  
 <211> 355  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(355)  
 <223> n = A,T,C or G

```
<400> 401
actgtttcca tgttatgttt ctacacattg ctacctcagt gctcctggaa acttagcttt 60
tgatgtctcc aagtagtcca ccttcattta actctttgaa actgtatcat ctttgccaag 120
taagagtggg gccctatttc agctgctttg acaaaatgac tggctcctga cttaacgttc 180
tataaatgaa tgtgctgaag caaagtgcc atggtggcgg cgaagaagan aaagatgtgt 240
tttgttttgg actctctgtg gtcccttcca atgctgnggg ttccaacca ggggaagggt 300
cccttttgca ttgccaagtg ccataacat gagcactact ctaccatggn tctgc 355
```

<210> 402  
 <211> 407  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(407)  
 <223> n = A,T,C or G

```
<400> 402
atggggcgaag ctggataaag aaccaagacc cactggagta tgcgtgtcttc aagaaacca 60
tctcacatgc ggtggcatag ataggctcaa aataaaggaa tggagaaaaa tatttcaagc 120
aaatggaaaa cagaaaaaag cagggtgttc actctactt tctgacaaaa cagactatgc 180
gaataaagat aaaaaagaga aggacattac aaaggtggtc ctgacctttg ataaatctca 240
ttgcttgata ccaacctggg ctgttttaat tgcccaaacc aaaaggataa tttgctgagg 300
ttgtggagct tctccccgc agagagtcct tgatctccca aaatttgggt gagatgtaag 360
gntgattttg ctgacaactc cttttctgaa gttttactca tttccaa 407
```

<210> 403  
 <211> 303  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(303)  
 <223> n = A,T,C or G

```
<400> 403
cagtatttat agccnaactg aaaagctagt agcaggcaag tctcaaattc aggcacaaaa 60
tcctaagcaa gagccatggc atggtgaaaa tgcaaaagga gagctctggcc aatctacaaa 120
tagagaacaa gacctactca gtcatgaaca aaaaggcaga caccaacatg gatctcatgg 180
gggattggat attgtaatta tagagcagga agatgacagt gatcgtcatt tggcacaaca 240
tcttaacaac gaccgaaacc cattatttac ataaacctcc attcggtaac catgttgaaa 300
gga 303
```

<210> 404  
<211> 225  
<212> DNA  
<213> Homo sapiens

<400> 404  
aagtgttaact tttaaaaatt tagtggattt tgaaaattct tagaggaaaag taaaggaaaa 60  
attgttaatg cactcattta cctttacatg gtgaaagttc tctcttgatc ctacaaacag 120  
acattttcca ctctgtgttc catagtgtt aagtgtatca gatgtgttgg gcatgtgaat 180  
ctccaagtgc ctgtgtaata aataaagtat ctttatttca ttcatt 225

<210> 405  
<211> 334  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(334)  
<223> n = A,T,C or G

<400> 405  
gagctgttat actgtgagtt ctactaggaa atcatcaaat ctgagggttg tctggaggac 60  
ttcaatacac ctccccccat agtgaatcag ctccaggagg gtccagtcct tctccttact 120  
tcatcccat cccatgccaa aggaagaccc tccctccttg gctcacagcc ttctctaggc 180  
ttcccagtgct ctccaggaca gagtgggtta tgttttcagc tccatccttg ctgtgagtggt 240  
ctggtgcggt tgtgcctcca gcttctgctc agtgcttcat ggacagtgtc cagcccatgt 300  
cactctccac tctctcanng tggatccac ccct 334

<210> 406  
<211> 216  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(216)  
<223> n = A,T,C or G

<400> 406  
tttcatacct aatgaggagg ttganatnac atnnaaccag gaaatgcatg gatctcaang 60  
gaaacaaaca cccaataaac tcggagtggc agactgacaa ctgtgagaca tgcacttgct 120  
acnaaacaca aatttnatgt tgcacccttg tttctacacc tgtgggttat gacaaagaca 180  
actgccaaag aatnttcaag aaggaggact gccant 216

<210> 407  
<211> 413  
<212> DNA  
<213> Homo sapiens

<400> 407  
gctgacttgc tagtatcatc tgcattcatt gaagcacaag aacttcatgc cttgactcat 60  
gtaaatgcaa taggattaaa aaataaattt gatatcacat ggaaacagac aaaaaatatt 120  
gtacaacatt gcaccagtg tcagattcta cacctggcca ctgaggagc aagagttat 180  
cccagaggct tatgtcctaa tgtgttatgg caaatggatg tcatgcacgt accttcattt 240

```
.ggaaaaattgt catttgtcca tgtgacagtt gatacttatt cacatttcat atgggcaacc 300
tgccagacag gagaaagtct tcccatgtta aaagacattt attatcttgt ttctctgtca 360
tgggagttcc agaaaaagt aaaacagaca atggggccagg ttctgtagta aag          413
```

```
<210> 408
<211> 183
<212> DNA
<213> Homo sapiens
```

```
<220>
<221> misc_feature
<222> (1)...(183)
<223> n = A,T,C or G
```

```
<400> 408
ggagctngcc ctcaattcct ccatntctat gttancatat ttaatgtcct ttgnnattaa 60
tntttaacta gttaatcctt aaagggctan ntaatcetta actagtccct ccattgtgag 120
cattatcctt scagtattcn ccttctnttt tatttactcc ttccctggcta cccatgtact 180
ntt                                     183
```

```
<210> 409
<211> 250
<212> DNA
<213> Homo sapiens
```

```
<220>
<221> misc_feature
<222> (1)...(250)
<223> n = A,T,C or G
```

```
<400> 409
cccacgcag ataagctctt tatttctgta agtccctgcta ggaaatcatc aaatctgacg 60
gtggtttggg ggacctgaac aaacctcctg taattaatca gctttcagtt tctcccccta 120
gtccctcctt caacaacata ggaggatcct cccctctctt ctgctcacgg ccttatctag 180
gcttcccagt gccccagga cagcgtgggc tatgtttaca gcgcntcctt gctggggggg 240
ggcctatgc                                     250
```

```
<210> 410
<211> 306
<212> DNA
<213> Homo sapiens
```

```
<220>
<221> misc_feature
<222> (1)...(306)
<223> n = A,T,C or G
```

```
<400> 410
ggctggtttg caagaatgaa atgaatgatt ctacagctag gacttaacct tgaatggaa 60
agtcttgcaa tccatttgc aggatccgtc tgtgcacatg cctctgtaga gagcagcatt 120
cccagggacc ttggaaacag ttggcactgt aagggtgctt ctccccaaga cacatcctaa 180
aagggtgtgt aatggtgaaa accgcttcct tctttattgc cccttcttat ttatgtgaac 240
nactggttgg ctttttttgn atctttttta aactggaaag ttcaattgng aaaatgaata 300
tcntgc                                     306
```

<210> 411  
 <211> 261  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(261)  
 <223> n = A,T,C or G

<400> 411  
 agagatattn cttaggtnaa agttcataga gttcccatga actatatgac tggccacaca 60  
 ggatcttttg tatttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120  
 tttaaatgtc tgaaatggaa cagatttcaa aaaaaaaccc cacaatctag ggtgggaaca 180  
 aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttaccat cagttccagc 240  
 cttctctcaa gngaggcaa a 261

<210> 412  
 <211> 241  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(241)  
 <223> n = A,T,C or G

<400> 412  
 gttcaatgtt acctgacatt tctacaacac cccactcacc gatgtattcg ttgccagtg 60  
 ggaacatacc agcctgaatt tggaaaaaat aattgtgttt ctgcccagg aaatactacg 120  
 actgactttg atggctccac aaacataacc cagtgtaaaa acagaagatg tggaggggag 180  
 ctgggagatt tctctgggta cattgaattc caaaactacc cangcaatta cccagccaac 240  
 a 241

<210> 413  
 <211> 231  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(231)  
 <223> n = A,T,C or G

<400> 413  
 aactcttaca atccaagtga ctcatctgtg tgcttgaatc ctttccactg tctcatctcc 60  
 ctcatccaag tttctagtac cttctctttg ttgtgaagga taatcaaact gaacaacaaa 120  
 aagtttactc tcctcatttg gaacctaaaa actctcttct tcctgggtct gagggctcca 180  
 agaatccttg aatcanttct cagatcattg gggacaccan atcaggaacc t 231

<210> 414  
 <211> 234  
 <212> DNA  
 <213> Homo sapiens

<400> 414  
actgtccatg aagcactgag cagaagctgg aggcacaacg caccagacac tcacagcaag 60  
gatggaggctg aaaacataac ccactctgtc ctggaggcac tgggaagcct agagaaggct 120  
gtgagccaag gagggagggt cttcctttgg catgggatgg ggatgaagta aggagaggga 180  
ctggaccccc tggaagctga ttcactatgg ggggagggtg attgaagccc tcca 234

<210> 415  
<211> 217  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(217)  
<223> n = A,T,C or G

<400> 415  
gcataaggatt aagactgagt atcttttcta cattctttta acttttctaag gggcacttct 60  
caaaacacag accaggtagc aaatctccac tgctctaagg ntctcaccac cactttctca 120  
accctagcaa tagtagaatt cagtcctact tctgaggcca gaagaatggg tcagaaaaat 180  
antggattat aaaaaataac aattaagaaa aataatc 217

<210> 416  
<211> 213  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(213)  
<223> n = A,T,C or G

<400> 416  
atgcatatnt aaagganact gcctcgcttt tagaagacat ctggnctgct cctgcgatga 60  
ggcacagcag taaagctctt tgattcccag aatcaagaac tctccccttc agactattac 120  
cgaatgcaag gtggttaatt gaaggccact aattgatgct caaatagaag gatattgact 180  
atattggaac agatggagtc tctactacaa aag 213

<210> 417  
<211> 303  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(303)  
<223> n = A,T,C or G

<400> 417  
nagtcttcag gcccatcagg gaagttcaca ctggagagaa gtcatacata tgtactgtat 60  
gtgggaaagg ctttactctg agttcaaata ttcaagccca tcagagagtc cacttgagag 120  
agaagccata caaatgcaat gagtgtggga agagcttcag gagggattcc cattatcaag 180  
ttcatctagt ggtccacaca ggagagaaac cctataaatg tgagatatgt gggaagggct 240  
tcantcaaag ttcgtatctt caaatccatc ngaaggncca cagtatanan aaacctttta 300  
agt 303



<210> 418  
 <211> 328  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(328)  
 <223> n = A,T,C or G

<400> 418  
 tttttggcgg tgggtggggca gggacggggac angagtctca ctctgttgcc caggctggag 60  
 tgcacaggca tgatctcggc tcaactacaac ccctgcctcc catgtccaag cgattcttgt 120  
 gcctcagcct tccctgtagc tagaattaca ggcacatgcc accacaccca gctagttttt 180  
 gtatttttag tagagacagg gtttcacccat gttggccagg ctggtctcaa actcctnacc 240  
 tcagnggtca ggctggtctc aaactcctga cctcaagtga tctgccacc tcagcctccc 300  
 aaagtgcctan gattacaggc cgtgagcc 328

<210> 419  
 <211> 389  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(389)  
 <223> n = A,T,C or G

<400> 419  
 ctcctccaag acggcctytg gtccgcctcc cggcaaccaa gaagcctgca gtgccatag 60  
 acccctgagc catggactgg agcctgaaag gcagcgtaca ccctgctcct gatcttgctg 120  
 cttgtttcct ctctgtggct ccattcatag cacagtgtgt gcactgaggc ttgtgcaggc 180  
 cgagcaaggc caagctggct caaagagcaa ccagtcaact ctgccacggg gtgccaggca 240  
 ccggttctcc agccaccaac ctactcgtct cccgcaaagt gcacatcagt tcttctaccc 300  
 taaaggtagg accaaagggc atctgctttt ctgaagtcct ctgctctatc agccatcacg 360  
 tggcagccac tcnggctgtg tcgacgcgg 389

<210> 420  
 <211> 408  
 <212> DNA  
 <213> Homo sapiens

<400> 420  
 gttcctccta actcctgccca gaaacagctc tcctcaacat gagagctgca cccctcctcc 60  
 tggccagggc agcaagcctt agccttggtc tcttgtttct gcttttttcc tggctagacc 120  
 gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180  
 gtcccattga cacttttccc actgacccca taaaggaaac ctcatggcca caaggatttg 240  
 gccaaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300  
 gatatagaaa attcttgaat gagtcttata aacatgaaca ggtttatatt cgaagcacag 360  
 acgttgaccg gactttgatg aagtgtctatg acaaacctgg caagcccg 408

<210> 421  
 <211> 352  
 <212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(352)

<223> n = A,T,C or G

<400> 421

```
gctcaaaaat ctttttactg atnggcatgg ctacacaatc attgactatt acggaggcca 60
gaggagaatg aggcctggcc tgggagccct gtgcctacta naagcacatt agattatcca 120
ttcactgaca gaacaggctc tttttgggtc cttcttctcc accacnatat acttgacgtc 180
ctccttcttg aagattcttt ggcagttgtc tttgtcataa cccacagggt tagaaacaag 240
ggtgcaacat gaaatttctg tttcgtagca agtgcatgtc tcacaagtgc gcangtctgc 300
cactccgagt ttattgggtg tttgtttcct ttgagatcca tgcatttcct gg 352
```

<210> 422

<211> 337

<212> DNA

<213> Homo sapiens

<400> 422

```
atgccaccat gctggcaatg cagcgggagg tcgaaggcct gcatatccag cccaagctgg 60
cgatgatcga cggcaaccgt tgcccgaagt tgccgatgcc agccgaagcg gtggtcaagg 120
gcatagacaa ggtgccggcg atcgccggcg cgtcaatcct ggccaaggct agccgtgac 180
gtgaaatggc agctgtcgaa ttgatctacc cgggttatgg catcgggcgg cataagggtc 240
atccgacacc ggtgcacctg gaagccttgc agcggctggg gccgacgcgg attcaccgac 300
gcttcttccg ccggtacggc tggcctatga aaatttat 337
```

<210> 423

<211> 310

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(310)

<223> n = A,T,C or G

<400> 423

```
gctcaaaaat ctttttactg atatggcatg gctacacaat cattgactat tagaggccag 60
aggagaatga ggccctggcct gggagccctg tgccctactan aagcncatta gattatccat 120
tcaactgacag aacaggctct ttttgggtcc ttcttctcca ccacgatata cttgcagtc 180
tccttcttga agattctttg gcagttgtct ttgtcataac ccacagggtg anaaacaagg 240
gtgcaacatg aaatttctgt ttcgtagcaa gtgcatgtct cacagttgtc aagtctgccc 300
tccgagttta 310
```

<210> 424

<211> 370

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(370)

<223> n = A,T,C or G

&lt;400&gt; 424

```

gctcaaaaat ctttttactg ataggcatgg ctacacaatc attgactatt agaggccaga 60
ggagaatgag gcctggcctg ggagccctgt gcctactaga agcacattag attatccatt 120
cactgacaga acagggtctt tttgggtcct tcttctccac cacgatatac ttgcagtcct 180
ccttcttgaa gattcttttg cagttgtctt tgtcataacc cacagggtga gaaacatcct 240
ggttgaatct cctggaactc cctcattagg tatgaaatag catgatgcat tgcataaagt 300
cacgaagggtg gcaaagatca caacgctgcc cagganaaca ttcattgtga taagcaggac 360
tccgtcgcagc
370

```

&lt;210&gt; 425

&lt;211&gt; 216

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (216)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 425

```

aattgctatn ntttattttg ccactcaaaa taattaccaa aaaaaaaaaa tnttaaatga 60
taacaacnca acatcaagggn aaananaaca ggaatggntg acntgtcata aatngggcca 120
anattatcca ttatnttaag ggttgacttc aggntacagc acacagacaa acatgcccag 180
gaggntntca ggaccgctcg atgtntntng aggagg
216

```

&lt;210&gt; 426

&lt;211&gt; 596

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 426

```

cttccagtgga ggataaccct gttgccccgg gccgagggtc tccattaggc tctgattgat 60
tggcagtcag tgatggaagg gtgttctgat cattccgact gccccaaggg tcgctggcca 120
gctctctgtt ttgctgagtt ggcagtagga cctaatttgt taattaagag tagatgggtga 180
gctgtccttg tattttgatt aacctaatgg ccttcccagc acgactcgga ttcagctgga 240
gacatcacgg caacttttaa tgaatgatt tgaagggccca ttaagaggca cttcccgtta 300
ttaggcagtt catctgcact gataacttct tggcagctga gctggtcgga gctgtggccc 360
aaacgcacac ttggcttttg gttttgagat acaactctta atcttttagt catgcttgag 420
ggtaggatggc cttttcagct ttaacccaat ttgcaactgcc ttggaagtgt agccaggaga 480
atacactcat atactcgtgg gcttagaggc cacagcagat gtcattggct tactgcctga 540
gtcccgcgtg tcccatccca ggaccttcca tcggcgagta cctgggagacc cgtgct
596

```

&lt;210&gt; 427

&lt;211&gt; 107

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (107)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 427

```

gaagaattca agttagggtt attcaaaggg cttacngaga atcctanacc caggncaccag 60

```

ccccgggagca gccttanaga gctcctgttt gactgcccgg ctcagng 107

<210> 428  
<211> 38  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(38)  
<223> n = A,T,C or G

<400> 428  
gaacttcena anaangactt tatttactat ttacatt 38

<210> 429  
<211> 544  
<212> DNA  
<213> Homo sapiens

<400> 429  
ctttgctgga cggaaataaaa gtggacgcaa gcatgacctc ctgatgaggg cgctgcattt 60  
attgaagagc ggtcgcagcc ctgcggttca gataaaaac cgagaattgt atagacgccg 120  
atatccacga actcttgaag gactttctga ttatccaca atcaaatcat cggttttcag 180  
tttgatggtt ggctcatcac ctgtagaacc tgacttggcc gtggctggaa tccactcgtt 240  
gccttcact tcagttacac ctcatcacc atcctctcct gttggttctg tgcgtcttca 300  
agataactaag cccacatttg agatgcagca gccatctccc ccaattcctc ctgtccatcc 360  
tgatgtgcag ttaaaaaatc tgccctttta tgatgtcctt gatgttctca tcaagccac 420  
gagtttagtt caaagcagta ttcagcgatt tcaagagaag ttttttatat ttgctttgac 480  
acctcaacaa gttagagaga tatgcatatc cagggtattt ttgccagggt gtaggagaga 540  
ttat 544

<210> 430  
<211> 507  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(507)  
<223> n = A,T,C or G

<400> 430  
cttatcncaa tggggctccc aaacttggtt gtgcagtga aactccgggg gaattttgaa 60  
gaacactgac acccatcttc caccgcgaca ctctgattta attgggtctg agtgagaaca 120  
gagcatcaat ttaaaaaagc gcccagaatg ttntcctggg cagcgttggt atctttgccn 180  
ccttcgtgac tttatgcaat gcacatgct atttcatacc taatgagggg gttccaggag 240  
attcaaccag gatgttttca cncctgtggg ttatgacaaa gacaactgcc aaagaatntt 300  
caagaaggag gactgcaagt atatcgtggt ggagaagaag gacccaaaaa agacctgttc 360  
tgtcagtga tggataatct aatgtgcttc tagtaggcac aggggtccca ggccaggcct 420  
cattctcctc tggcctctaa tagtcaatga ttgtgtagcc atgcctatca gtaaaaagat 480  
ttttgagcaa aaaaaaaaaa aaaaaaa 507

<210> 431  
<211> 392

<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(392)  
<223> n = A,T,C or G

<400> 431  
gaaaattcag aatggataaa aacaaatgaa gtacaaaata ttccagattt acatagcgat 60  
aaacaagaaa gcacttatca ggaggactta caaatggaag tacactctan aaccatcatc 120  
tatcatggct aaatgtgaga ttagcacagc tgtattattt gtacattgca aacacctaga 180  
aagagatggg aaacaaaatc ccaggagttt tgtgtgtgga gtccctgggtt ttccaacaga 240  
catcattcca gcattctgag attagggnga ttggggatca ttctggagtt ggaatgttca 300  
acaaaagtga tgttgttagg taaaatgtac aacttctgga tctatgcaga cattgaaggt 360  
gcaatgagtc tggctttttac tctgctgttt ct 392

<210> 432  
<211> 387  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(387)  
<223> n = A,T,C or G

<400> 432  
ggatccnta cataatcaaa tatagctgta gtacatgttt tcattggngt agattaccac 60  
aaatgcaagg caacatgtgt agatctcttg tcttattctt ttgtctataa tactgtattg 120  
ngtagtccaa gctctcggn a gtccagccac tngaaacat gctcccttta gattaacctc 180  
gtggacnctn ttgttgnatt gtctgaactg tagngccctg tattttgtct ctgtctgnga 240  
attctgttgc ttctggggca ttcccttgng atgcagagga ccaccacaca gatgacagca 300  
atctgaattg ntccaatcac agctgcgatt aagacatact gaaatcgtac aggaccggga 360  
acaacgtata gaacactgga gtccttt 387

<210> 433  
<211> 281  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(281)  
<223> n = A,T,C or G

<400> 433  
ttcaactagc anagaanact gcttcagggn gtgtaaaatg aaaggcttcc acgcagttat 60  
ctgattaaag aacactaaga gagggacaag gctagaagcc gcaggatgtc tacactatag 120  
caggcnctat ttgggttggc tggaggagct gtggaaaaca tggagagatt ggcgctggag 180  
atcgccgttg ctattctctn ttgntattac accagngagg ntctctgtnt gccactgggt 240  
tnnaaaaccg ntatacaata atgatagaat aggacacaca t 281

<210> 434  
<211> 484

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 434

```
ttttaaaata agcatttagt gctcagtcct tactgagtag tctttctctc cctctctctg 60
aatttaattc tttcaacttg caatttgcaa ggattacaca tttcactgtg atgtatatgt 120
tgttgcaaaa aaaaaaaagt gtctttgttt aaaattactt ggtttgtaga tccatctgtc 180
tttttcccca ttggaactag tcattaaccc atctctgaac tggtagaaaa acatctgaag 240
agctagtcta tcagcatctg acagggtgaat tggatgggtc tcagaacccat ttcacccaga 300
cagcctgttt ctatcctgtt taataaatta gtttgggttc tctacatgca taacaaaccc 360
tgctccaatc tgtcacataa aagtctgtga cttgaagttt agtcagcacc cccaccaaac 420
tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataaag taccatgtc 480
ttta 484
```

&lt;210&gt; 435

&lt;211&gt; 424

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 435

```
gcgcccgtca gagcagggtc ctttctgcct tccacgtcct ctttcaagga agccccatgt 60
gggttagcttt caatatcgca gggtcttact cctctgcctc tataagctca aaccacccaa 120
cgatcgggca agtaaacccc ctccctcgcc gacttcggaa ctggcgagag ttcagcgag 180
atgggcctgt ggggaggggg caagatagat gagggggagc ggcatgggtc ggggtgaccc 240
cttggagaga ggaaaaaggc cacaagaggg gctgccaccg ccactaacgg agatggccct 300
ggtagagacc tttgggggtc tggaaacctc ggactcccca tgctctaact cccacactct 360
gctatcagaa acttaaaactt gaggattttc tctgttttct actcgcaata aattcagagc 420
aaac 424
```

&lt;210&gt; 436

&lt;211&gt; 667

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)... (667)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 436

```
accttgggaa nactctcaca atataaaggg tcgtagactt tactccaaat tccaaaaagg 60
tcctggccat gtaatcctga aagttttccc aaggtagcta taaaatcctt ataagggtgc 120
agcctcttct ggaattctct tgatttcaaa gtctcactct caagttcttg aaaacgaggg 180
cagttctctga aaggcaggta tagcaactga tcttcagaaa gaggaactgt gtgcaccggg 240
atgggctgcc agagtaggat aggattccag atgctgacac cttctggggg aaacaggggt 300
gccaggtttg tcatagcact catcaaaagtc cgggtcaacgt ctgtgcttcg aatataaac 360
tgttcatgtt tataggactc attcaagaat tttctatatc tcttcttat atactctca 420
agttcataat gctgctccat gccacgtcgg gtgagttggc caaatccttg tgcccatgag 480
gattccttta tggggtcagt gggaaaagggt tcaatgggac ttccgtctcc atgccgaaac 540
accaaagtca caaacttcaa ctccctggct agtacacttc ggtctagcca gaaaaaaagc 600
agaaacaaga agccaaggct aaggcttgct gccctgccag gaggaggggt gcagctctca 660
tgttag 667
```

&lt;210&gt; 437

&lt;211&gt; 693

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 437

```

ctacgtctca accctcattt ttaggtaagg aatcttaagt ccaagatat taagtgactc 60
acacagccag gtaaggaaag ctggattggc acactaggac tctaccatac cgggttttgt 120
taaagctcag gttaggaggc tgataagctt ggaaggaaact tcagacagct ttttcagatc 180
ataaaagata attcttagcc catgttcttc tccagagcag acctgaaatg acagcacagc 240
aggtaactct ctattttcac cctctctgct tctactctct ggcagtcaga cctgtgggag 300
gccatgggag aaagcagctc tctggatgtt tgtacagatc atggactatt ctctgtggac 360
catttctcca ggttacccta ggtgtcacta ttggggggac agccagcatc tttagctttc 420
atttgagttt ctgtctgtct tcagtagagg aaacttttgc tcttcacact tcacatctga 480
acacctaact gctgttgctc ctgaggtggt gaaagacaga tatagagctt acagtattta 540
tcctatttct aggcactgag ggctgtggg taccttgttg tgccaaaaca gatcctgttt 600
taaggacatg ttgtctcaga gatgtctgta actatctggg ggctctgttg gctctttacc 660
ctgcatcatg tgctctcttg gctgaaatg acc 693

```

&lt;210&gt; 438

&lt;211&gt; 360

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 438

```

ctgcttatca caatgaatgt tctcctgggc agcgttgtga tctttgccac ctctgtgact 60
ttatgcaatg catcatgcta ttctataact aatgagggag ttccaggaga ttcaaccagg 120
atgtttctac acctgtgggt tatgacaaag acaactgcca aagaatcttc aagaaggagg 180
actgcaagta tatctggttg agaagaagga cccaaaaaag acctgttctg tcagtgaatg 240
gataatctaa tgtgtctcta gtaggcacag ggctcccagg ccaggcctca tctcctctg 300
gcctctaata gtcaataatt gtgtagccat gcctatcagt aaaaagattt ttgagcaaac 360

```

&lt;210&gt; 439

&lt;211&gt; 431

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(431)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 439

```

gttctnnta actcctgcc aacacagctc tctcaacat gagagctgca cccctctctc 60
tggccagggc agcaagcctt agccttggct tcttgtttct gcttttttct tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgacttttgt gtttcggcat ggagaccgaa 180
gtcccattga cacttttccc actgacccca taaaggaaatc ctcatggcca caaggatttg 240
gccaaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaaga 300
gatatagaaa attcttgaat gagtcttata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg agtgctatga caaacctggc agcccgctga cgcggccgcg 420
aatttagtag t 431

```

&lt;210&gt; 440

&lt;211&gt; 523

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 440

```

agagataaag cttaggtcaa agttcataga gttcccatga actatatgac tggccacaca 60
ggatccttttg tatttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120
tttaaatgtc tgaaatggaa cagatttcaa aaaaaaaccc cacaatctag ggtgggaaca 180
aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttaccat cagttccagc 240
cttctctcaa ggagaggcaa agaaaggaga tacagtggag acatctggaa agttttctcc 300
actggaaaac tgctactatc tgtttttata ttctgttaa aatatatgag gctacagaac 360
taaaaattaa aacctctttg tgtcccttgg tcctggaaca tttatgttcc ttttaaagaa 420
acaaaaatca aactttacag aaagatttga tgtatgtaat acatatagca gctcttgaag 480
tatatatatc atagcaata agtcatctga tgagaacaag cta 523

```

&lt;210&gt; 441

&lt;211&gt; 430

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 441

```

gttcctccta actcctgcc aaaaacagctc tcctcaacat gagagctgca cccctcctcc 60
tggccagggc agcaagcctt agccttggtt tcttgtttct gcttttttcc tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180
gtcccatgga cacttttccc actgacccca taaaggaatc ctcatggcca caaggatttg 240
gccaaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attccttgaat gagtcctata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg agtgctatga caaacctggc agcccgtcga cgcggccgcg 420
aatttagtag 430

```

&lt;210&gt; 442

&lt;211&gt; 362

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 442

```

ctaaggaaatt agtagtgttc ccatcacttg ttggagtggt gctattctaa aagattttga 60
tttcctggaa tgacaattat attttaactt tgggtgggga aagagttata ggaccacagt 120
cttcacttct gatacttgta aattaatctt ttattgcact tgttttgacc attaatgctat 180
atgtttagaa atgggtcattt tacggaaaaa ttagaaaaat tctgataata gtgcagaata 240
aatgaattaa tgttttactt aatttatatt gaactgtcaa tgacaaataa aaattctttt 300
tgattatttt ttgttttcat ttaccagaat aaaaactaag aattaaaagt ttgattacag 360
tc 362

```

&lt;210&gt; 443

&lt;211&gt; 624

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(624)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 443

```

tttttttttt gcaacacaat atacatcaca gtgaaatgtg taatccttgc aaattgcaag 60
ttgaaagaat taaattcaga ggaggggaga gaaagagtag tcagtaggga ctgagcacta 120
aatgcttatt ttaaaagaaa tgtaaaagagc agaaagcaat tcaggctacc ctgccttttg 180
tgctggctag tactccggct ggtgtcagca gcacgtggca ttgaacattg caatgtggag 240

```



```
cccaaacac agaaaaatggg gtgaaattgg ccaactttct attaacttgg ctccctgttt 300
tataaaatat tgtgaaataat atcacctact tcaaagggca gttatgaggc ttaaataaac 360
taacgcctac aaaacacctta aacatagata acataggtgc aagtactatg tatctgtgtac 420
atggtaaac tcccttattat taaagtcaac gctaaaatga atgtgtgtgc atatgctaata 480
agtacagaga gagggcactt aaaccaacta agggcctgga gggaagggtt cctggaaga 540
ngatgcttgt gctgggtcca aatcttgggc tactatgacc ttggcccaaat tatttaaact 600
ttgtccctat ctgctaaaca gatac 624
```

```
<210> 444
<211> 425
<212> DNA
<213> Homo sapiens
```

```
<220>
<221> misc_feature
<222> (1)...(425)
<223> n = A,T,C or G
```

```
<400> 444
gcacatcatt nntcttgcatt tcttttgagaa taagaagatc agtaaatagt tcagaagtgg 60
gaagctttgt ccagggcctgt gtgtgaaccc aatgttttgc tttagaaatag aacaagtaag 120
ttcatttgcta tagcataaca caaaatttgc ataagtgggtg gtcagcaaat ccttgaatgc 180
tgcttaaatgt gagaggttgg taaaaacctt tgtgcaacac tctaactccc tgaatgtttt 240
gctgtgctgg gacctgtgca tgccagacaa ggccaagctg gctgaaagag caaccagcca 300
cctctgcaat ctgccacctc ctgctggcag gatttgtttt tgcactctgt gaagagccaa 360
ggaggcacca gggcataagt gagtagactt atggtcgacg cggccgcgaa ttagtagta 420
gtaga 425
```

```
<210> 445
<211> 414
<212> DNA
<213> Homo sapiens
```

```
<220>
<221> misc_feature
<222> (1)...(414)
<223> n = A,T,C or G
```

```
<400> 445
catgtttatg ntthttggatt actttgggca cctagtgttt ctaaatcgtc tatcattctt 60
ttctgttttt caaaagcaga gatggccaga gtctcaacaa actgtatctt caagtctttg 120
tgaattctct tgcattgtggc agattattgg atgtagtctt cttaacttag catataaatc 180
tggtgtgttt cagataaatg aacagcaaaa tgtggtggaa ttaccattttg gaacatttgt 240
aatgaaaaat tgtgtctcta gattatgtaa caaataacta tttcctaacc attgatcttt 300
ggatttttat aatcctactc acaaatgact aggccttctc tcttgatttt tgaagcagtg 360
tgggtgctgg attgataaaa aaaaaaaaag tcgacgcggc cgcgaattta gtac 414
```

```
<210> 446
<211> 631
<212> DNA
<213> Homo sapiens
```

```
<220>
<221> misc_feature
<222> (1)...(631)
```

<223> n = A,T,C or G

<400> 446

```
acaaattaga  anaaagtgcc  agagaacacc  acataccttg  tccggaacat  tacaatggct  60
tctgcatgca  tgggaagtgt  gagcattcta  tcaatatgca  ggagccatct  tgcaggtgtg  120
atgctggtta  tactggacaa  cactgtgaaa  aaaaggacta  cagtgttcta  tacgttgttc  180
ccggtcctgt  acgatttcag  tatgtcttaa  tcgcagctgt  gattggaaca  attcagattg  240
ctgtcatctg  tgtgtgtgtc  ctctgcatca  caagggccaa  accttaggta  atagcattgg  300
actgagattt  gtaaaacttt  caaccttcca  ggaatgccc  cagaagcaac  agaattcaca  360
gacagaagca  aaatacaggg  cactacagtt  cagacaatac  aacaagagcg  tccacgaggt  420
taatctaaag  ggagcatgtt  tcacagtggc  tggactaccg  agagcttgga  ctacacaata  480
cagtattata  gacaaaagaa  taagacaaga  gatctacaca  tgttgccctg  catttgtggt  540
aatctacacc  aatgaaaaca  tgtactacag  ctatatttga  ttatgcatgg  atatatttga  600
aatagtatac  attgtcttga  tgtttttct  g  631
```

<210> 447

<211> 585

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(585)

<223> n = A,T,C or G

<400> 447

```
ccttgggaaa  antntcacaa  tataaagggt  cgtagacttt  actccaaatt  ccaaaaagg  60
cctggccatg  taatcctgaa  agttttccca  aggragctat  aaaatcctta  taagggtgca  120
gcctcttctg  gaattcctct  gatttcaaag  tctcactctc  aagtctctga  aaacgagggc  180
agttcctgaa  aggcaggtat  agcaactgat  cttcagaaa  aggaactgtg  tgcaccggga  240
tgggctgcca  gagtaggata  ggattccaga  tgctgacacc  ttctggggga  aacagggctg  300
ccaggtttgt  catagcactc  atcaaagtcc  ggtcaacgtc  tgtgcttcga  atataaacct  360
gttcagtgtt  ataggactca  ttcaagaatt  ttctatatct  ctttcttata  tactctccaa  420
gttcataatg  ctgctccatg  cccagctggg  tgagttggcc  aaatccttgt  ggccatgagg  480
attcctttat  ggggtcagtg  ggaaagggtg  caatgggact  tcggtctcca  tgccgaaaca  540
ccaaagtcac  aaacttcaac  tccttggtca  gtacacttcg  gtcta  585
```

<210> 448

<211> 93

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(93)

<223> n = A,T,C or G

<400> 448

```
tgctcgtggg  tcattctgan  nccgaactg  acctgccag  ccctgccgan  gggccnccat  60
ggctccctag  tgccctggag  aggangggc  tag  93
```

<210> 449

<211> 706

<212> DNA

<213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(706)  
 <223> n = A,T,C or G

<400> 449  
 ccaagttcat gctntgtgct ggacgctgga cagggggcaa aagcnnntgc tcgtgggtca 60  
 ttctgancac cgaactgacc atgccagccc tgccgatggt cctccatggc tccctagtgc 120  
 cctggagagg aggtgtctag tcagagagta gtccctggaag gtggcctctg ngaggagcca 180  
 cggggacagc atcctgcaga tggctcggcg cgtcccattc gccattcagg ctgcgcaact 240  
 gttgggaagg gcgatcggtg cgggcctctt cgctattacg ccagctggcg aaagggggat 300  
 gtgctgcaag gcgattaagt tgggtaacgc cagggttttc ccagtcncca cgttgtaaaa 360  
 cgacggccag tgaattgaat ttaggtgacn ctatagaaga gctatgacgt cgcatgcacg 420  
 cgtacgtaag cttggatcct ctgagcggcg cgccactac tactaaattc gcggccgcgt 480  
 cgacgtggga tcncactga gagagtggag agtgacatgt gctggacnct gtcctatgaag 540  
 cactgagcag aagctggagg cacaacgcnc cagacactca cagctactca ggaggctgag 600  
 aacaggttga acctgggggg tggagggttc aatgagctga gatcaggccn ctgcncccca 660  
 gcatggatga cagagtgaat ctccatctta aaaaaaaaa aaaaaa 706

<210> 450  
 <211> 493  
 <212> DNA  
 <213> Homo sapiens

<400> 450  
 gagacggagt gtcactctgt tgcccaggct ggagtgcagc aagacactgt ctaagaaaaa 60  
 acagttttta aaggtaaaac aacataaaaa gaaatatact atagtggaaa taagagagtc 120  
 aaatgaggct gagaacttta caaagggatc ttacagacat gtcgccaata tcaactgcatg 180  
 agcctaagta taagaacaac ctttggggag aaaccatcat ttgacagtga ggtacaattc 240  
 caagtcaagt agtgaaatgg gtggaattaa actcaaatca atcctgccag ctgaaacgca 300  
 agagacactg tcagagagtt aaaaagttag ttctatccat gaggtgatcc cacagtcttc 360  
 tcaagtcaac acatctgtga actcacagac caagtctcta aaccactgtt caaactctgc 420  
 tacacatcag aatcacctgg agagctttac aaactcccat tgccgagggt cgacgcggcc 480  
 gcgaatttag tag 493

<210> 451  
 <211> 501  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(501)  
 <223> n = A,T,C or G

<400> 451  
 gggcgctgcc cattcgccat tcaggctgcg caactgttgg gaaggcgat cggtgcgggc 60  
 ctcttcgcta ttacgcaccg tggcgaaagg gggatgtgct gcaaggcgat taagttgggt 120  
 aacgccaggg ttttcccagt cncgacgttg taaaacgacg gccagtgaat tgaatttagg 180  
 tgacnctata gaagagctat gacgtcgcat gcacgcgtac gtaagcttgg atcctctaga 240  
 gcggccgcct actactacta aattcgcggc cgcgtcgacg tgggatccnc actgagagag 300  
 tggagagtga catgtgcttg acnctgtcca tgaagcactg agcagaagct ggaggcacia 360  
 cgcncacagc actcacagct actcaggagg ctgagaacag gttgaacctg ggagggtgag 420  
 gttgcaatga gctgagatca ggccnctgcn cccagcagat gatgacagag tgaaactcca 480

tcttaaaaaa aaaaaaaaaa a

501

&lt;210&gt; 452

&lt;211&gt; 51

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(51)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 452

agacgggttc accnttaciaa cnccttttag gatgggnntt ggggagcaag c

51

&lt;210&gt; 453

&lt;211&gt; 317

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(317)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 453

tacatcttgc tttttcccca ttggaactag tcattaaccc atctctgaac tggtagaaaa 60  
acatctgaag agctagtcta tcagcatctg gcaagtgaat tggatgggttc tcagaaccat 120  
ttcacccana cagcctgttt ctatcctggt taataaatta gtttgggttc tctacatgca 180  
taacaaaccc tgctccaatc tgtcacataa aagtctgtga cttgaagttt antcagcacc 240  
cccacaaac tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataagg 300  
taccatgtc tttatta 317

&lt;210&gt; 454

&lt;211&gt; 231

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 454

ttcgaggtac aatcaactct cagagtgtag tttccttcta tagatgagtc agcattaata 60  
taagccacgc cagctctctg aaggagtctt gaattctcct ctgctcactc agtagaacca 120  
agaagaccaa attctctgct atcccagctt gcaaacaaaa ttgttctctt aggtctccac 180  
ccttcctttt tcagtgttcc aaagctcctc acaatttcat gaacaacagc t 231

&lt;210&gt; 455

&lt;211&gt; 231

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 455

taccaagag ggcataataa tcagtctcac agtaggggtc accatcctcc aagtgaaaaa 60  
cattgttccg aatgggcttt ccacaggcta cacacacaaa acaggaaaca tgccaagttt 120  
gtttcaacgc attgatgact tctccaagga tcttcctttg gcatcgacca cattcagggg 180  
caaagaatth ctcatagcac agctcacaat acagggtctc tttctcctct a 231

<210> 456  
<211> 231  
<212> DNA  
<213> Homo sapiens

<400> 456  
ttggcaggta cccttacaaa gaagacacca taccttatgc gttattaggt ggaataatca 60  
ttccattcag tattatcggt attattcttg gagaaaccct gtctgtttac tgtaaccttt 120  
tgcactcaaa ttccctttatc aggaataact acatagccac tatttacaaa gccattggaa 180  
cctttttatt tgggtgcagct gctagtcagt ccctgactga cattgccaaag t 231

<210> 457  
<211> 231  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)... (231)  
<223> n = A,T,C or G

<400> 457  
cgaggatccc aggggtctga aaatctctnn ttctantagtc gatagcaaaa ttgttcatca 60  
gcattccctta atatgatctt gctataatta gattttttctc cattagagtt catacagttt 120  
tatttgattt tattagcaat ctctttcaga agacccttga gatcattaag ctttgtatcc 180  
agttgtctaa atcgatgcct catttcctct gaggtgtcgc tggcttttgc g 231

<210> 458  
<211> 231  
<212> DNA  
<213> Homo sapiens

<400> 458  
aggtctggtt cccccactt ccactccct ctactctctc taggactggg ctggggccaag 60  
agaagagggg tgggttagga agccgttgag acctgaagcc ccacctctca ccttccctca 120  
acaccctaac cttgggtaac agcatttgga attatcattt gggatgagta gaatttccaa 180  
ggtcctgggt taggcatttt ggggggccag accccaggag aagaagattc t 231

<210> 459  
<211> 231  
<212> DNA  
<213> Homo sapiens

<400> 459  
ggtaccgagg ctgcgtgaca cagagaaacc ccaacgcgag gaaaggaatg gccagccaca 60  
ccttcgcgaa acctgtggtg gccaccagct cctaaccgga caggacagag agacagagca 120  
gcctgcact gttttccctc caccacagcc atcctgtccc tcattggctc tgtgctttcc 180  
actatacaca gtcaccgtcc caatgagaaa caagaaggag caccctccac a 231

<210> 460  
<211> 231  
<212> DNA  
<213> Homo sapiens

<400> 460

```
gcaggataaa catgctgcaa caacagatgt gactaggaac ggccgggtgac atggggagggg 60
ccatcacccc tattcttggg ggctgcttct tcacagtgat catgaagcct agcagcaaat 120
cccacctccc cacacgcaca cggccagcct ggagcccaca gaaggggtcct cctgcagcca 180
gtggagcttg gtccagcctc cagtccacc ctagcaggct taaggataga a 231
```

&lt;210&gt; 461

&lt;211&gt; 231

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 461

```
cgaggtttga gaagctctaa tgtgcagggg agccgagaag caggcggcct agggagggtc 60
gcgtgtgttc cagaagagtg tgtgcatgcc agaggggaaa caggcgccctg tgtgtcctgg 120
gtggggttca gtgaggagtg ggaaatttgt tcagcagaac caagccgttg ggtgaataag 180
agggggattc catggcactg atagagccct atagtttcag agctgggaat t 231
```

&lt;210&gt; 462

&lt;211&gt; 231

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 462

```
aggtaccctc attgtagcca tgggaaaatt gatgttcagt ggggatcagt gaattaaatg 60
gggtcatgca agtataaaaa ttaaaaaaaa aagacttcat gcccaatctc atatgatgtg 120
gaagaactgt tagagagacc aacagggttag tgggttagag atttccagag tcttacattt 180
tctagaggag gtatttaatt tcttctcact catccagtgt tgtatttagg a 231
```

&lt;210&gt; 463

&lt;211&gt; 231

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 463

```
tactccagcc tggtagacaga gcgagaccct atcaccgccc cccacccccc caaaaaaaaa 60
actgagtaga cagggtgtcct cttggcatgg taagtcttaa gtcccctccc agatctgtga 120
catttgacag gtgtcttttc ctctggacct cgggtgtcccc atctgagtga gaaaaggcag 180
tggggagggtg gatcttccag tcgaagcggg atagaagccc gtgtgaaaag c 231
```

&lt;210&gt; 464

&lt;211&gt; 231

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 464

```
gtactctaag attttatcta agttgccttt tctgggtggg aaagtttaac cttagtgtact 60
aaggacatca catatgaaga atgtttaagt tggaggtggc aacgtgaatt gcaaacaggg 120
cctgtctcag tgactgtgtg cctgtagtcc cagctactcg ggagtctgtg tgaggccagg 180
ggtgccacg caccagctag atgctctgta acttctaggc cccattttcc c 231
```

&lt;210&gt; 465

&lt;211&gt; 231

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 465

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&lt;210&gt; 466

&lt;211&gt; 231

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 466

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&lt;210&gt; 467

&lt;211&gt; 311

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 467

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&lt;210&gt; 468

&lt;211&gt; 3112

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 468

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&lt;210&gt; 469

&lt;211&gt; 2229

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 469

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&lt;210&gt; 470

&lt;211&gt; 2426

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 470

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&lt;210&gt; 471

&lt;211&gt; 812

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 471

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812

&lt;210&gt; 472

&lt;211&gt; 515

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

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&lt;223&gt; n = A,T,C or G

&lt;400&gt; 472

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## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification 7 :</b> <b>C12N 15/12, C07K 14/47, C12Q 1/68, A61K 39/395, G01N 33/68, 33/574, C07K 16/30, C12N 15/62, 5/02 // A61P 35/00</b>	<b>A3</b>	<b>(11) International Publication Number: WO 00/04149</b>  <b>(43) International Publication Date: 27 January 2000 (27.01.00)</b>
<b>(21) International Application Number:</b> PCT/US99/15838  <b>(22) International Filing Date:</b> 14 July 1999 (14.07.99)  <b>(30) Priority Data:</b> 09/115,453 14 July 1998 (14.07.98) US 09/116,134 14 July 1998 (14.07.98) US 09/159,822 23 September 1998 (23.09.98) US 09/159,812 23 September 1998 (23.09.98) US 09/232,880 15 January 1999 (15.01.99) US 09/232,149 15 January 1999 (15.01.99) US 09/288,946 9 April 1999 (09.04.99) US  <b>(71) Applicant:</b> CORIXA CORPORATION [US/US]; Suite 200, 1124 Columbia Street, Seattle, WA 98104 (US).  <b>(72) Inventors:</b> DILLON, Davin, Clifford; 21607 N.E. 24th Street, Redmond, WA 98053 (US). HARLOCKER, Susan, Louise; 6203 20th Avenue N.W., Seattle, WA 98107 (US). YUQIU, Jiang; 5001 South 232nd Street, Kent, WA 98032 (US). XU, Jiangchun; 15805 S.E. 43rd Place, Bellevue, WA 98006 (US). MITCHAM, Jennifer, Lynn; 16677 Northeast 88th Street, Redmond, WA 98052 (US).	<b>(74) Agents:</b> MAKI, David, J. et al.; Seed and Berry LLP, 6300 Columbia, 701 Fifth Avenue, Seattle, WA 98104-7092 (US).  <b>(81) Designated States:</b> AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).  <b>Published</b> <i>With international search report.</i>  <b>(88) Date of publication of the international search report:</b> 20 July 2000 (20.07.00)	
<b>(54) Title:</b> COMPOSITIONS AND METHODS FOR THERAPY AND DIAGNOSIS OF PROSTATE CANCER  <b>(57) Abstract</b>  <p>Compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer, are disclosed. Compositions may comprise one or more prostate tumor proteins, immunogenic portions thereof, or polynucleotides that encode such portions. Alternatively, a therapeutic composition may comprise an antigen presenting cell that expresses a prostate tumor protein, or a T cell that is specific for cells expressing such a protein. Such compositions may be used, for example, for the prevention and treatment of diseases such as prostate cancer. Diagnostic methods based on detecting a prostate tumor protein, or mRNA encoding such a protein, in a sample are also provided.</p>		

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## INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 99/15838

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/12 C07K14/47 C12Q1/68 A61K39/395 G01N33/68  
 G01N33/574 C07K16/30 C12N15/62 C12N5/02  
 //A61P35/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 97 33909 A (CORIXA CORP) 18 September 1997 (1997-09-18)  the whole document  ---	1-22, 29-31, 35-49, 53-79
A	SJOGREN H O: "Therapeutic immunization against cancer antigens using genetically engineered cells" IMMUNOTECHNOLOGY, vol. 3, no. 3, 1 October 1997 (1997-10-01), pages 161-172, XP004097000 ISSN: 1380-2933 the whole document  ---	23-28, 32-34, 53-57
	--- -/-	

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents:

\*A\* document defining the general state of the art which is not considered to be of particular relevance

\*E\* earlier document but published on or after the international filing date

\*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

\*O\* document referring to an oral disclosure, use, exhibition or other means

\*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*Z\* document member of the same patent family

Date of the actual completion of the international search

31 January 2000

Date of mailing of the international search report

04.05.00

Name and mailing address of the ISA

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ANDRES S.M.

## INTERNATIONAL SEARCH REPORT

International Application No

PC1, JS 99/15838

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>CHU R S ET AL: "CPG OLIGODEOXYNUCLEOTIDES ACT AS ADJUVANTS THAT SWITCH ON T HELPER 1 (TH1) IMMUNITY" JOURNAL OF EXPERIMENTAL MEDICINE, vol. 186, no. 10, 1 November 1997 (1997-11-01), pages 1623-1631, XP002910130 ISSN: 0022-1007 the whole document ---</p>	<p>14-20, 25-27, 41-47</p>
A	<p>EP 0 317 141 A (BECTON DICKINSON CO) 24 May 1989 (1989-05-24) the whole document ---</p>	<p>50-52</p>
A	<p>ZITVOGEL L ET AL: "Eradication of established murine tumors using a novel cell-free vaccine: dendritic cell-derived exosomes" NATURE MEDICINE, vol. 4, no. 5, 1 May 1998 (1998-05-01), pages 594-600, XP002085387 ISSN: 1078-8956 cited in the application ---</p>	
P,X	<p>WO 98 37093 A (CORIXA CORP) 27 August 1998 (1998-08-27)  page 3, line 20 -page 22, line 2 page 35, line 9 - last line page 76, line 34 -page 78, line 22 claims ---</p>	<p>1-15, 17-19, 21,22, 29-31, 34,35, 39-42, 44-46, 48,49, 58-79</p>
P,X	<p>WO 98 37418 A (CORIXA CORP) 27 August 1998 (1998-08-27)  page 2 -page 24 example 2 page 35, line 15 -page 36, line 11 page 81, line 14 -page 83, line 11 claims -----</p>	<p>1-15, 17-19, 21,22, 29-31, 34,35, 39-42, 44-46, 48,49, 58-79</p>

# INTERNATIONAL SEARCH REPORT

In ternational application No.

PCT/US 99/ 15838

## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
Remark: Although claims 29-34, 48-49, 52, 55-57  
are directed to a method of treatment of the human/animal  
body, the search has been carried out and based on the alleged  
effects of the compound/composition.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such  
an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all  
searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment  
of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report  
covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is  
restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-79 all partially

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.



## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

## Invention 1. Claims: 1-79 (all partially)

A polypeptide comprising at least an immunogenic portion of a prostate tumor protein defined as SEQ ID 108 and which is encoded by the related SEQ IDs 2,3,107 (according to the Description of the Sequence Identifiers), fragments and variants thereof, fusion proteins comprising it, polynucleotides or oligonucleotides derived therefrom, antibodies or fragments thereof binding to the polypeptide, pharmaceutical compositions or vaccines comprising these products and their use in methods for inhibiting, monitoring or diagnosing the development of a prostate cancer, for removing tumor cells from a sample or for expanding and/or stimulating T-cells.

Inventions 2. to 439. Claims: 1-79 (all partially and as far as applicable)

As for subject 1. but concerning respectively SEQ IDs 1,4-106,109-111,115-171,173-175,177,179-305,307-315,326,328, 330,332-335,340-375,381,382 and 384-472.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PC1, JS 99/15838

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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